University of Alberta

Prevalence, incidence and risk factors of asthma and wheezing in children from Yukon, Nunavut and Northwest Territories

by

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Dedication

To Dr. A. Senthilselvan,
who gave me this opportunity

Abstract

Prevalence and incidence rates of asthma and wheeze, and associated factors were determined using the National Longitudinal Study of Children and Youth-North. Aboriginal infants and toddlers had significantly greater prevalence of current-wheeze (22.1%) than non-Aboriginal infants and toddlers (12.1%). In school-age children, incidence of wheeze and asthma were significantly greater in non-Aboriginals (5.3%, 3.2%) than in Aboriginals (3.2%, 1.8%). Maternal history of asthma was a significant risk factor for prevalence and incidence of asthma, and incidence of wheeze. Being infants and toddlers, number of siblings and mother's smoking habit were significant risk factors for prevalence and incidence of wheeze. Child's allergic history was a significant risk factor for asthma prevalence and wheeze incidence. Dwelling ownership was significantly associated with prevalence of asthma while mother's education and total household income were significantly associated with incidence of wheeze. High attrition during the follow-up restricts generalization of results from the incidence study.

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Table of Contents

		Page
Chapter 1:	**Introduction**	1
Chapter 2:	**Literature Review**	4
2.1	Asthma prevalence and incidence in Canadian population	4
2.2	Asthma prevalence and incidence in American Indians	6
2.2.1	Canadian aboriginal population	6
2.2.2	Asthma prevalence in Canadian aboriginal population	6
2.2.3	Asthma prevalence in American Indians	7
2.3	Asthma etiology	7
2.3.1	Physical exercise	7
2.3.2	Tobacco smoking and passive smoking exposure	8
2.3.3	Birth weight, head circumference and gestational age	10
2.3.4	Maternal age	12
2.3.5	Breast-feeding	12
2.3.6	Atopy	14
2.3.7	Parental atopy	15
2.3.8	Dust mite exposure, pets, damp and mould in home	16
2.3.9	Exposure to infectious agents	17
2.4	Summary	18
Chapter 3:	**Objectives**	20
Chapter 4:	**Methods**	21
4.1	Objectives of NLSCY-North	21
4.2	Sample	22
4.3	Sample size	22
4.4	Data collection	22
4.5	Interviewing	23
4.6	Non-response	23
4.7	Sample weighting	23
4.8	Variables and definitions in this study	24
4.8.1	Variable list	24
4.8.2	Asthma related questions in the questionnaire	25

4.9 Statistics methods..... 25
4.9.1 Cross-sectional analysis..... 25
4.9.2 Longitudinal analysis..... 26
4.9.3 Purposeful selection methods..... 27
4.10 Identification of asthma and wheezing related literature..... 27

Chapter 5: Results..... 28

5.1 Descriptive results..... 28

5.2 Asthma and wheeze prevalence..... 33

5.3 Risk factors of asthma and wheeze prevalence..... 40
5.3.1 Risk factors of prevalence of ever-asthma..... 40
5.3.2 Univariate analysis for risk factors of prevalence of current-wheeze..... 41
5.3.3 Confounding effects of mother smoking habit in prevalence of current-wheeze..... 42

5.4 Asthma and wheeze incidence..... 50
5.4.1 Descriptive results..... 52
5.4.2 Risk factors of asthma incidence..... 53
5.4.3 Risk factors of wheeze incidence..... 53

Chapter 6: Discussion and conclusion..... 66

6.1 Validity of the current study..... 66

6.2 Asthma and wheeze prevalence..... 67

6.3 Risk factors of prevalence of asthma and wheeze..... 70

6.4 Asthma and wheeze incidence..... 74

6.5 Risk factors of incidence of asthma and wheeze..... 74

6.6 Limitations..... 75

6.7 Conclusion..... 76

References..... 78

Appendix..... 88

List of tables

Page

Table 1: Distribution of households by number of children..... 29

Table 2: Age distributions of children in the three territories..... 30

Table 3: Racial distributions of children in the three territories..... 30

Table 4: Gender distributions of children in the three territories..... 31

Table 5: Distributions of children by age and gender..... 31

Table 6: Distributions of children by race and age groups..... 31

Table 7: Distributions of children by race and gender..... 32

Table 8: Distributions of children by race, age and gender..... 32

Table 9: Univariate analysis for risk factors of prevalence of ever-asthma..... 43

Table 10: Effect modifiers, confounders of race for prevalence of ever-asthma..... 44

Table 11: Multivariate analysis for prevalence of ever-asthma..... 45

Table 12: Stratification by race in multivariate logistic regression..... 45

Table 13: Univariate analysis for risk factors of prevalence of current wheeze..... 46

Table 14: Effect modifiers, confounders of race for prevalence of current wheeze. 47

Table 15: Multivariate analyses for the prevalence of current wheeze..... 48

Table 16: Stratification by race in multivariate analysis..... 48

Table 17: Confounding effects of mother smoking habit..... 49

Table 18: Comparison between those who completed more than one cycle and those who completed only the first cycle 51

List of tables (continued)

Table 19: Univariate analysis for risk factors of asthma incidence..... 60

Table 20: Multivariate analysis of asthma incidence in Poisson model..... 62

Table 21: Univariate analysis for risk factors of wheeze incidence..... 63

Table 22 Multivariate analysis for risk factors of wheeze incidence..... 65

List of figures

Page

Figure 1: Prevalence of ever-asthma, current-asthma and current-wheeze by three territories..... 35

Figure 2: Prevalence of ever-asthma, current-asthma and current-wheeze in three age groups..... 36

Figure 3: Prevalence of ever-asthma, current-asthma and current-wheeze by race..... 36

Figure 4: Prevalence of ever-asthma, current-asthma and current-wheeze by gender..... 37

Figure 5: Prevalence of ever-asthma by race and age..... 37

Figure 6: Prevalence of current-asthma by race and age..... 38

Figure 7: Prevalence of current-wheeze by race and age..... 38

Figure 8.1: Prevalence of current wheeze by race age and gender..... 39

Figure 8.2: Prevalence of ever-asthma by race, age and gender..... 39

Figure 9: Asthma and wheeze incidence by race..... 54

Figure 10: Asthma and wheeze incidence by age. 54

Figure 11: Asthma and wheeze incidence by gender..... 55

Figure 12: Asthma and wheeze incidence in the three territories..... 55

Figure 13.1: Asthma incidence by race and gender..... 56

Figure 13.2: Wheeze incidence by race and gender..... 56

Figure 14.1: Asthma incidence by race and territories..... 57

Figure 14.2: Wheeze incidence by race and territories..... 57

Figure 15.1: Asthma incidence by race and age..... 58

Figure 15.2: Asthma incidence by race and age..... 58

Figure 16.1: Asthma incidence by race, age and gender..... 59

Figure 16.2: Wheeze incidence by race, age and gender..... 59

Chapter 1

Introduction

Asthma has remained a puzzle to patients and physicians from the time of Hippocrates to the present days. It is one of the most common chronic disorders affecting children and adults. According to the International Study of Asthma and Allergies in Childhood (ISAAC), worldwide prevalence of asthma varied between 1.3% to 30.8% in the children aged 6 to 7 years, and 1.4% to 30.2% in the children aged 13 to 14 years in 1996 (ISAAC Steering Committee, 1998). In the ISAAC study, prevalence of asthma was higher in developed countries than in developing countries. In Canada, the prevalence of asthma was 12.2% in children and youth less than 20 years of age, and 14% among the children aged 15-19 years, and was higher in the Eastern Provinces than in the Western Provinces (Public Health Agency of Canada, 1999; Dales et al, 1994). There has been an increase in asthma prevalence in the 1980s and early part of 1990s, but recent studies, investigating temporal trends, have indicated an apparent stabilization in asthma prevalence in the late 1990s and from 2000 to 2004 (Lawson et al, 2005; Senthilselvan, 2003).

In a review of admissions from 1946 to 1963 to a hospital in Edmonton, Canada, only three cases of asthma were identified in Aboriginal population (Herxheimer et al, 1974). In the Province of Saskatchewan, Canada, hospitalization rates were greater in preschool children and older adults among Aboriginal population in comparison to non-Aboriginal population from 1980 to 1989 (Senthilselvan, 1995). This pattern was also observed in a recent study from Saskatchewan in which younger and older Aboriginal population had had greater asthma prevalence than non-

Aboriginal population from 1991 to 1998 (Senthilselvan, 2003). In USA, researchers in a retrospective analysis of Washington State hospitalization data from 1987 to 1996 reported that American Indian and Alaska Native children aged more than 1 year were 2 to 3 times more likely to be hospitalized due to asthma and bronchiolitis in comparison to other ethnic groups (Liu, 2000). In a study conducted in Hartford, Connecticut, USA, using National, State, and Municipal reports from 1998 to 2000, the highest asthma prevalence was reported to be in Hispanic/Puerto Rican children aged 0 to 18 years (Cloutier et al, 2002). Another study, investigating bronchial hyper-responsiveness and allergic levels in African-American and European-American children of ages 6 to 8 years in Detroit, USA, reported that African-American children were more reactive to methacholine challenge test, and had significantly higher total IgE than European-American children indicating that African-American children were at higher risk of developing asthma (Joseph et al, 2000).

Even though many epidemiological studies have shown that asthma is related to both genetic and environmental factors, the factors, which are associated with asthma, are still poorly understood. In addition to differences in genetic factors, lifestyle and cultural factors also differ between Aboriginal and non-Aboriginal populations in Canada. These differences raise the possibility that factors associated with prevalence and incidence of asthma might be different between the two populations. In this research project, asthma and wheeze prevalence in Aboriginal population living in the three Northwest Territories is reported as well as their determinants. Only a few studies have examined the prevalence of asthma and wheeze in Canada.

Research data

Data collected by the Statistics Canada in Yukon, Nunavut and Northwest Territories were used in this thesis. The longitudinal nature of this survey, National Longitudinal Survey of Children and Youth-North (NLSCY-North) allowed of estimations of asthma and wheeze incidence and their determinants in Aboriginal and non-Aboriginal populations residing in the three territories. Moreover, broad aspects of information covered in the NLSCY-North allowed of determination of host, parental and household factors associated with incidence of asthma and wheeze in Aboriginal and non-Aboriginal children aged 0 to 11 years living in the three Territories.

Chapter 2

Literature review

Asthma is one of the most common chronic diseases among children. The causal factors of asthma are still poorly understood, especially in marginalized populations. However, international comparisons of prevalence and characteristics of asthma have been greatly facilitated by two major population based studies, the European Commission Respiratory Health Study (Burney et al, 1994) in adults and the ISAAC (ISAAC Steering Committee, 1998) in children.

According to the 1995 National Health Interview Survey, more than 17 million Americans suffered from asthma. At least 5.3 million were under age of 18 years, making asthma the leading chronic illness in children (American Lung Association, 2000). The total direct and indirect cost estimates for asthma in 1994 amounted to $5.82 billion (Smith et al, 1997). The direct costs were about 88% and the indirect costs were about 12% of the total. Hospitalizations represented the single greatest cost category, accounting for 54% of the total direct costs at $2.80 billion. The next largest expenditure was outpatient visits, accounting for 23% of the total direct costs at $1.18 billion. Medication costs were lower, representing 16% of the total direct costs at $817 million (Smith et al, 1997). Nocturnal awakening, sleep disruption and activity limitation due to asthma symptoms, are common problems for persons suffering from asthma (Turner-Warwick, 1988; Pianosi et al, 2004).

2.1 Asthma prevalence and incidence rate in Canadian population

Asthma prevalence had been increasing in the 1980s and early part of 1990s but recent studies have indicated an apparent stabilization in asthma prevalence in late

1990s and from 2000 to 2004 (Lawson and Senthilselvan, 2005; Garcia-Marcos et al, 2004; Senthilselvan et al, 2003).

In the 1980s and early part of 1990s, asthma prevalence was inexplicably increasing among children in both developed and developing countries including Canada, USA (Mannino et al, 1998; Millar et al, 1999; Sears, 1991), and China (Chen, 2004; The ISAAC Steering Committee, 1998). Variations have also been reported in asthma prevalence within a province and between provinces in Canada (Miller et al, 1999). Miller et al (1999) also reported that among the children aged 0 to 14 years, asthma prevalence was slightly greater in Atlantic region (14%) than in other regions of Canada. Asthma prevalence varied between 10% to 12% in Quebec, Ontario, Prairies, and British Columbia. In the ISAAC study of children aged 6 to 7 years and 13 to 14 years living in Hamilton, Ontario and Saskatoon, Saskatchewan, cumulative asthma prevalence varied between the two cities, with Hamilton children having higher rate than Saskatoon children (6-7 yr: 17.2% vs 11.2%; 13-14 yr: 19.2% vs 12.2%) (Habbick et al, 1999). In a school-based survey of 28,029 students aged 5 to 19 years in nine voluntary health unit/department areas across Canada, asthma prevalence varied between 10% and 18% with higher rates reported in Prince Edward Island (18%), Halifax (17%) and Kingston (16%), and lower rates (10% to 13%) reported in health unit areas in Sherbrooke, Guelph, Winnipeg, Saskatoon, Edmonton, and Kelowna (Health Canada, 1998).

Only a few studies have been conducted to investigate incidence rates of asthma among Canadian population. A recent study of physician-diagnosed asthma in children during their first six years of life in the Province of Manitoba, Canada reported that the incidence rate of asthma was 14.1% in the study period (Dik et al, 2004). In this study, boys were at significantly higher risk of developing asthma than

girls, and children living in the urban areas were at significantly higher risk than those living in the rural areas (Dik et al, 2004).

2.2 Asthma prevalence and incidence rate in American Indians

2.2.1 Canadian Aboriginal Population

In the 1996 Canadian Census, 799,010 (2.80%) of the 28.5 million Canadian populations were of aboriginal ancestry, which was comprised of 554,290 North American Indians, 210,190 Metis, and 41,080 Inuits (Statistics Canada, 2002). About 62% of the Aboriginal population resided in Western Canada, 18% in Ontario, 9% in Quebec, 5% in Eastern Canada, and 6% in the Yukon and Northwest Territories. In Yukon, about 20% of the total population (30,650) was of Aboriginal ancestry which included 90% North American Indians, 9% Metis and 1% Inuits. More than half the population (62%) of Northwest Territories was of Aboriginal ancestry (39,690) which included 29% North American Indians, 10% Metis and 61% Inuits.

2.2.2 Asthma prevalence in Canadian Aboriginal population

There are limited epidemiological studies of asthma prevalence in Canadian Aboriginal population. A study conducted in the Province of Saskatchewan, Canada, reported the increasing trends in asthma hospitalizations in preschool children and older adults among Aboriginal population (Senthilselvan et al, 1995). In another study of Inuit school children in Northern Quebec, 6.0% of the children had parental-report of wheezing in the previous 12 months and 5.3% had evidence of atopy (Hemmelgarn et al, 1997). Incidence rats of asthma are not known among Canadian Aboriginal population.

2.2.3 Asthma prevalence in American Indians

Only a few studies have reported asthma prevalence in American Indians. In a study of prevalence of chronic respiratory symptoms among the Alaska Native and American Indian middle school students from sixth to ninth grades in Western Alaska 7.4% of the children reported physician-diagnosed asthma, and 11.4% had prevalence of asthma-like symptoms without a diagnosis of asthma (Lewis et al, 2004). In an analysis of 1987 Survey of American Indians and Alaska Native children of ages 1 to 17 years, the prevalence of asthma was 7.07%, which was slighter lower than the prevalence for the US population (Stout et al, 1999). Using the Washington State hospitalization data for 1987 to 1996, the hospitalization rates for asthma and bronchiolitis among Alaska Native and American Indian children older than one year were 2 to 3 times higher than the rates for children of other races combined (Liu et al, 2000).

2.3 Asthma etiology

A review of risk factors of asthma, which have been previously investigated, is given in the following sections.

2.3.1 Physical exercise

Regular participation of physical exercise can be helpful to increase lung function in young people. A study of adolescents aged 13-19 years in Norway showed a positive dose-response relationship between physical exercise involvement and lung function (forced vital capacity and forced expiratory volume in one second, adjusted for age and height) among non-smokers (Holmen et al, 2002).

Disappearance of traditional ways of life among some Aboriginal people has led

to a more sedentary lifestyle. Health Canada in 1999 reported that in early 1990s only 18.8% of Northwest Territories Inuit males between the ages of 13 and 39 years and 11.6% of women between the ages of 13 and 29 years were physically active (Health Canada, 1999). Lack of involvement in physical activities among Aboriginal people, especially the young people, also poses risks for a variety of health problems apart from asthma (e.g., diabetes, heart disease, etc).

Vigorous exercise can also induce asthma exacerbations. Exercise induced asthma (EIA) is defined as "transient narrowing of the airways that follows vigorous exercise" (Anderson et al, 2000). It does not produce a long-term increase in airway reactivity. It has been reported to be more prevalent in child and young people because of their higher levels of physical activity (Makker et al, 1994). The EIA frequently goes undiagnosed. Approximately 9% of individuals with the EIA have no history of asthma or allergy (Mehta et al, 1997). A study of 1998 US winter Olympic members of the US team showed that exercise induced bronchospasm was prevalent in several Olympic winter sports and affected nearly one in every four elite winter sport athletes, emphasizing that this condition could be found even in well-conditioned individuals who appear to be in excellent health (Wilber, 2000).

2.3.2. Tobacco smoking and Passive smoking exposure

Several studies have shown that parental cigarette smoking, especially maternal smoking, was a significant risk factor of asthma and wheeze in children. In a longitudinal study of asthma in Tucson, Arizona, 763 children were followed from birth to age 3 and 6 years (Martinez et al, 1995). In this study, 52.9% had no history of wheezing and 19.3% had transient wheezing by three years, 14.7% developed wheezing at 6 years and 13.1% had wheezing at 3 ad 6 years. Maternal smoking was

associated with two times higher incidence rates of the transient and persistent wheezing only among the children aged 0 to three years, but showing less association with incidence rates of the later onset wheezing (Martinez et al, 1995). In a British birth cohort study, the association between maternal smoking and incidence rates of wheezing was also reported, in which the cumulative incidence rate of wheezing increased in the child with maternal smoking after adjusting for sex, birth weight, and breast-feeding (Lewis, 1996). A study of children (6-7 years) and adolescents (13-14 years) in Italy showed that parental smoking was related with asthma and wheezing in children and maternal smoking was a significant risk factor of current asthma symptoms including wheezing in children (Agabiti et al, 1999). More recently, a study of 6,611 school children aged 6 to 7 years in the Republic of Trinidad and Tobago showed that even in tropical countries where people spend most of their time outdoor and houses have more ventilation, parental smoking at home was strongly associated with increased asthma in pre-school child (Monteil et al, 2004).

There have been extensive studies on effects of tobacco smoke exposure on childhood asthma, particularly when the mother is a smoker (EPI, 1983; DHHS, 1986; NRC, 1986; Samet et al, 1996). These findings largely depended on parental reporting or self-reporting of smoking habits. There is also evidence showing that tobacco smoke exposure can increase severity of asthma in both children and adults (Mannino et al, 2002; Althuis et al, 1999).

Higher smoking rates among Aboriginal communities have been one of the biggest problems to their health and the health of their children. A study conducted in Canada reported that almost 62% of First Nations and Labrador Inuit individuals 15 years of age or older smoked (Reading et al, 1999), which was more than two times higher than 29% of smoking rate reported for general Canadian population in 1996-

1997 (Statistics Canada, 1998). Moreover, studies have also shown that Aboriginal children were more likely to start cigarette smoking at younger ages. It was reported that First Nations and Labrador Inuit children started to smoke as early as 6 to 8 years of age, with a rapid increase at ages 11 and 12 and a peak at age 16 (Reading et al, 1999). Cigarette smoking in pregnancy is also more common in Aboriginal women than non-Aboriginal women. In a study of pregnant women in Saskatoon, health risk behaviors (alcohol intake, tobacco use, the use of psychoactive drugs, caffeine intake) during early pregnancy were more prevalent among the women with Aboriginal or Métis background (Health Canada, 1999). A similar conclusion was also drawn in another study demonstrating that smoking, caffeine intake and binge drinking were more prevalent in Inuit and Indian pregnant women, compared to Caucasian women and those with mixed races (Godel et al, 1992). A recent study comparing of smoking habits of Aboriginal mothers and non-Aboriginal mothers while breastfeeding in Perth, Australia showed that prior to and during pregnancy, 67% of the Aboriginal and 18.3% of the Non-Aboriginal mothers smoked regularly (Giglia et al, 2004). A slight decline in smoking rate with the increasing length of breast-feeding was seen among the Aboriginal women (Giglia et al, 2004). In contrast, there was a decrease in the number of smokers in non-Aboriginal women during pregnancy (Giglia et al, 2004).

2.3.3. Birth weight, head circumference and gestational age

A number of epidemiological studies have investigated the association between perinatal factors and asthma. Birth weight, head circumference and gestation age have been routinely measured and well recorded in birth records. These perinatal factors are commonly used in epidemiological studies as potential risk factors for asthma. In a Norwegian study of 868 randomly selected young adults, birth weights

were inversely associated with prevalence of asthma, with an odds ratio (OR) = 0.69 [95% confidence interval (CI): 0.50-0.95] per 500g increase in the birth weight after adjustment for gestational age, birth length, parity and maternal age (Svanes et al, 1998). The researchers in this study concluded that the risk for asthma might be partly established early in life and suggested that poor intrauterine growth play an important role in the etiology of asthma. In another birth cohort study of 5,192 subjects born in Northern Finland, increased gestational age (over 40 weeks) was 1.65 times more likely to suffer atopy compared with normal gestational age (36 weeks), (OR = 1.65; 95% CI: 1.16, 2.34) (Pekkanen et al, 2001). Godfrey et al in their study of 280 men and women born at a single hospital in England reported a strong relationship between raised total serum IgE concentration in adult life and increased head circumference at birth, independently of gestational age at birth, birth weight, and the mother's pelvic size and parity (Godfrey et al, 1994).

However, some studies have shown that birth weight was positively related with increased asthma incidence among Aboriginal children, and Aboriginal children were at increased risk for developing asthma than non-Aboriginal children because of their increased birth weights (Sin, 2004). In a recent cohort study examining the relationship between birth weight of all neonates born at term (> or =37 weeks) and emergency visits for asthma during 10 years of follow-up in Alberta, Canada, Aboriginal children were significantly at higher risk for emergency visits (relative risk = 1.20; 95% CI, 1.11-1.29) in comparison to the non-Aboriginal child, and the relationship between higher birth weight (>4.5 kg) and the risk of emergency visits for asthma was linear, with 10% increase in the risk of emergency visits for asthma for every 100g increment in the birth weight (Sin, 2004). The proportion of babies with birth weight greater than 4,000 grams was higher among both males (22%) and

females (14%) in the First Nation and Inuit population in comparison to male (16%) and female (8%) babies in the general Canadian population (Statistics Canada, NLSCY, 1996; Statistics Canada. Births, 1998; British Columbia Vital Statistics Agency, 1998).

2.3.4. Maternal age

Several studies have shown that infants of younger mothers were at greater risk of developing asthma (Martinez et al, 1992; Schwartz et al, 1990). In the Tucson study, incidence of physician-diagnosed wheezing increased significantly ($p=0.005$) with decreasing maternal age (Martinez et al, 1992). Similar results were also reported in a study of children aged 6 months to 11 years of age in the Second National Health and Nutritional Examination Survey in the United States (Schwartz et al, 1990).

Studies have shown that maternal age of Aboriginal women tended to be younger than the general Canadian population (Dyck et al, 2002; Luo et al, 2004). A study of 2,006 women living in the Saskatoon Health District, showed that the mean maternal age of the Aboriginal women was 25.0 years (SD = 6.0 years), and they were significantly younger than the non-Aboriginal women, for whom the mean age was 28.5 years (SD = 5.3 years) (Dyck et al, 2002). In another study of Inuit, North American Indian and other ethnic women living in Quebec between 1985 and 1997, mean maternal age of the Aboriginal women was significantly lower than other ethnic groups (Inuit: 23.6; Indian: 23.8; French: 27.5; English: 28.7 years) (Luo et al, 2004).

2.3.5. Breast-feeding

Some studies have shown that breast feeding is highly protective against asthma

in children, while others have shown no effects (Hide et al, 1994; Saarinen et al, 1995) or even positively associated with asthma (Arshad et al, 1992; Lilja et al, 1989). There is evidence that prolonged breast feeding can reduce early childhood infections (Wright et al, 1989; Beaudry et al, 1995). Methodological issues in these studies may play a role in leading to these inconsistent results, such as differences in definition of breast-feeding and asthma, and in the age of the child when the outcome was diagnosed. A prospective birth cohort study of 4,089 infants in Stockholm, Sweden reported that exclusive breast feeding for four months or more reduced the risk of allergic symptoms up to 2 years of age and this protective effect was also observed even when children had several allergic disorders (Park et al, 1986). In the Tucson longitudinal study, breastfeeding was a protective factor in children at 6 years (Wright et al, 1995), whereas it was a risk factor in children at 13 years (Wright et al, 2001). This association was also observed in another large Italian study, in which breastfeeding reduced the risk of wheezing in infants less than two years old but increased the risk of late onset wheeze (Rusconi et al, 1999). However, in another birth cohort study conducted in New Zealand, researchers were unable to demonstrate the benefits of breast-feeding in reduction in the risk for asthma (Horwood et al, 1985).

Aboriginal women were reported to be less likely to breast-feed their children, but once they breast-fed their children, they tended to breast-feed for relatively longer time than Canadian general population. According to the First Nations and Inuit Regional Health Survey, 54% of children up to 2 years of age had been breast-fed, compared to 75% of children reported in the 1994-95 NLSCY for the Canadian general population, and of the First Nations and Inuit children who had been breast-fed, 39% had been breast-fed for over six months, compared to only 24% of the

children in the NLSCY (MacMillan et al, 1999; Statistics Canada, NLSCY, 1996).

2.3.6 Allergy

It has become routine to describe asthma as an allergic disease and has been well recognized that allergen exposure triggers atopic sensitization and continued exposure leads to clinical asthma through development of airways inflammation, bronchial hyper-responsiveness, and reversible airflow obstruction. The most commonly used diagnosis tests are high serum total IgE, allergen-specific serum IgE and positive skin-prick test to common allergens.

Many studies have reported that pediatric asthma is strongly associated with allergy. The longitudinal German Multi-center Allergy Study (MAS) reported that children with sensitization to food and/or inhalant common allergens (egg, milk, soy, wheat, cat and dog dander, house mite, birch and grass pollen) during the first 3 years of life were at significantly higher risk of asthma at 7 years of age than the child with early transient or no sensitization, OR = 10.12, 95% CI: 3.81-26.88 (Nickel et al, 2002). In another analysis of this study, children with atopic dermatitis and wheeze during the first 3 years were almost 3 times the risk of having current wheeze at age 7 years in comparison to children without early atopic dermatitis, OR = 2.84, 95% CI: 1.54-5.24. (Illi et al, 2004). Atopy was also reported to be strongly associated with pediatric asthma in countries where the prevalence of asthma is very low. In a study of 10,902 school children aged 9-11 years in China using the ISAAC questionnaire, researchers reported that atopic sensitization and skin-prick tests, were important risk factors associated with asthma in Chinese children (Wong et al, 2001). Child's allergic history was also reported to have a strong association with pediatric asthma among children from ethnic minority groups. A study of a representative sample of

4,164 United States children aged 6 to 16 years who participated in allergen testing in the Third National Health and Nutrition Examination Survey from 1988 to 1994 concluded that African American and Mexican American children were substantially more likely than Caucasian children to be sensitized to the allergens important in asthma (Stevenson et al, 2001).

Although asthma and allergy are closely related to each other, they also occur independently of each other. In a study of the role of atopy in asthma, defining skin-prick test positive as atopy, found that overall about 58% of children and 54% of adults with asthma were skin prick test positive; however, about 29% of non-asthmatic children and 24% of non-asthmatic adults were skin prick test positive and that the proportion of asthmatic attributable to atopy was only 38% in children and 37% in adults (Neil et al, 1999). In another birth cohort study in Western Australia, researchers found that allergy was more prevalent among children with asthma (55.5%) than children without asthma (38.3%) at 6 years (Oddy et al, 2002).

2.3.7 Parental allergy

Although environment factors have been showed to play a vital role in the development and exacerbation of asthma, many studies have consistently revealed family cluster patterns showing important genetic component in the study of asthma etiology (Turner, 1987; Litonjua et al, 1988). Asthma is known to be associated with allergy, as measured by serum IgE levels or skin test reactivity to allergens. Children of atopic parents are at greater risk of developing allergy and asthma than children of non-atopic parents (Litonjua et al, 1988). An ongoing longitudinal birth-cohort study in Boston found that among children younger than 5 years of age, the risk for childhood asthma associated with maternal asthma (OR = 5.0, 95% CI =1.7 to 14.9)

was greater than the risk associated with paternal asthma (OR = 1.6, 95% CI = 0.5 to 5.9), whereas asthma in both parents was associated with increased risk among children older than 5 years of age (OR = 4.6, 95% CI = 1.1 to 19.0 and OR = 4.1, 95% CI = 1.0 to 16.0, respectively), and the odds of having a child with asthma were three times greater in families with one asthmatic parent and six times greater in families with two asthmatic parents than in families where only one parent had inhalant allergy without asthma (Litonjua et al, 1988). Twin studies permit us to analyze the effects of environment risk factors, independent of genetic factors, without knowing the specific genes involved. One twin study of children in Finish found that asthma cases with at least one asthmatic parent, genetic factors could explain 87 percent of the variation in susceptibility to asthma in twins. Among families in which none of the parent had asthma, asthma incidence was explained more by environmental factors than genetic factors (Rasanen et al, 2000; Laitinene et al, 1998).

2.3.8. Dust mite exposure, pets, damp and mould in home

In a study conducted in the UK, 94% of children with asthma had skin sensitivity to allergens in comparison to 30% in those without asthma (Sporik et al, 1990). Damp and mould in home has been frequently reported to be associated with an increased prevalence of asthma (Lindfors et al, 1995; Strachan et al, 1989; Brunekreef et al, 1989). In a case-control study in Denmark using newly diagnosed asthma and randomly selected controls, asthma cases lived in older and more humid homes than the controls (Korsgard et al, 1983).

Etzel et al. reviewed several environmental factors and concluded that indoor air exposures were more strongly linked to the increase in asthma prevalence than other factors, and exposure to dust mites was a risk factor not only for the development of

asthma but also might exacerbate existing asthma (Etzel et al, 2003).

Aboriginal children are at increased risk of exposure to indoor allergens because majority of these children live in crowded and older homes. According to the 1996 Census, Aboriginal homes were over four times more likely to need major repairs than non-band dwellings (37% versus 8%, respectively) (Statistics Canada, 1996). The 2001 Census data also showed that Aboriginal children aged 14 and under were nearly twice as likely as all Canadian children to live in crowded conditions (Statistics Canada, 2001).

2.3.9 Exposure to infectious agents

Several epidemiological studies showed that children living in more affluent and more hygienic environment were more likely to develop atopic diseases than children raised in disadvantaged environment (Crane et al, 1989; Von et al, 1992; Bjorksten et al, 1994; Bjorksten, 2004). It has been reported that particular makeup of the microbial intestinal flora could effect immune system's deviation (Bjorksten, 2004). Among allergic children, lactobacilli and bifido-bacteria are less seen in microbial intestinal flora but higher counts of aerobic micro-organisms such as coliforms. The microenvironment of the intestinal flora might be associated with some of well known risk factors for asthma such as family size, number of older siblings, breastfeeding, day-care use, antibiotic use, exposure to household pets and farm living.

Some studies have showed that increased family size and day care attendance to be protective against asthma and allergic sensitization (Beasley et al, 2000). These two risk factors might be important indicators for increased exposure to infectious agents. The Tucson study found that children with exposure to other children at home or at day care were more likely to have frequent wheezing at age of two years than

children with little or no exposure, but were less like to have frequent wheezing from age of 6 years to age of 13 years (Ball et al, 2000). In this study, asthma prevalence was 21 percent in the children with no older sibling, 19 percent in the children with one older sibling, 14 percent in the children with two older siblings, and 13 percent in the children with more than three older siblings. They concluded that young children exposed to older children at home or to other children at day care might be more protective against development of asthma and frequent wheezing later in childhood. Similar conclusion was drawn in another study revealing that the first-borns were at a higher risk of allergen-specific IgE, OR = 1.92, 95% CI=1.16:3.18 and positive skin-prick tests at 6 years of age OR = 1.68, 95% CI=1.02-2.75 (Johnson et al, 2002).

The site of viral infections may be of importance for developing asthma. Results from Tasmanian study demonstrated that increased household size was associated with a greater risk of upper respiratory tract infections (OR = 1.77, 95% CI= 1.07-2.94) but not lower respiratory tract infections (Ponsonby et al, 1999). The Western Australia Pregnancy Cohort Study revealed that lower respiratory tract infections in first year of life were associated with an increased risk of current asthma (OR= 3.84, 95% CI= 2.82-5.24) (Oddy et al, 2002). Similar results were also found in the MAS study, in which the lower respiratory tract infections was a risk factor for the subsequent development of asthma, but episodes of runny nose at early age was negatively associated with the later development of asthma (Illi et al, 2001).

2.4. Summary

Asthma is a very common chronic disease in children. Unfortunately, the causal factors of asthma are still largely unclear. Recent epidemiological studies have confirmed that the causes of asthma are multifaceted, and are related to a variety of

risk factors, such as cultural, environmental, lifestyle and genetic factors. Aboriginal and non-Aboriginal Canadians have completely different culture and lifestyles. This provides us with an excellent opportunity to explore how these risk factors are associated with asthma among the Aboriginal population.

Asthma prevalence with increasing trends in the 1980s and early part of 1990s started to show an apparent stabilization in the late 1990s and from 2000 to 2004 (Lawson et al, 2005). Few studies have been conducted to determine asthma prevalence in Canadian Aboriginal population. The incidence rates of asthma among Aboriginal children are unknown.

Some the cultural and lifestyle factors in Aboriginal communities make this population at a higher risk of developing asthma. Aboriginal people, especially young Aboriginal people are not physically active have high rates of tobacco smoking and alcohol drinking and even pregnant Aboriginal women have high alcohol and tobacco consumption. Increased birth weight among Aboriginal newborn babies, younger maternal age and lower breast-feeding rates in Aboriginal women might be associated with asthma incidence and prevalence of asthma in Aboriginal children. Moreover, higher rates of poor housing conditions and overcrowded living situations in Aboriginal communities might also play a role in incidence and prevalence of asthma in Aboriginal children.

The primary objective of this study is to determine prevalence, incidence and risk factors of asthma and wheezing in Aboriginal children.

Chapter 3

Objectives

The objectives of the thesis are:

- to determine the prevalence of asthma and wheezing in Aboriginal and non-Aboriginal children aged 0 to 11 years living in Yukon, Nunavut and Northwest Territories using the data from first (cycle 1) National Longitudinal Survey of Children and Youth of North (NLSCY-North) conducted in 1994-95;
- to determine the predictors of asthma and wheezing prevalence in Aboriginal and non-Aboriginal children aged 0 to 11 years living in Yukon, Nunavut and Northwest Territories using the data from NLSCY-North cycle 1;
- to determine the incidence of asthma and wheezing incidence in Aboriginal and non-Aboriginal children using NLSCY-North cycle 1 (1994-95), cycle 2 (1996-97) and cycle 3 (1998-99);
- to determine the predictors of asthma and wheezing incidence in Aboriginal and non-Aboriginal children using NLSCY-North cycle 1, cycle 2 and cycle 3.

The null hypotheses to be tested in the thesis are:

- In age group 0 to 4 years, prevalence and incidence of asthma and wheezing will be greater in Aboriginal children than non-Aboriginal children;
- In age group 5 to 11 years, prevalence and incidence of asthma and wheezing will be similar in Aboriginal and non-Aboriginal schooling children;
- Parental and household factors will have greater predictive power of asthma and wheezing in Aboriginal children than in non-Aboriginal children;
- Predictors of asthma and wheezing prevalence and incidence will be different between Aboriginal and non-Aboriginal populations.

Chapter 4

Methods

This chapter describes the design and data collection of NLSCY and the statistical analysis used in this study.

The National Longitudinal Survey of Children and Youth-North (NLSCY-North) was used to address the research questions proposed in this thesis. The NLSCY-North is a long-term survey designed to measure child development and well-being (Statistic Canada, 1996). The first cycle of the survey was conducted by the Statistics Canada in 1994-1995 on behalf of the Human Resources Development of Canada.

4.1. Objectives of NLSCY-North:

The primary objective of the NLSCY-North is to develop a database on the characteristics and life experiences of children and youth living in the three territories in Canada as they grow from infancy to adulthood (Statistic Canada, 1996). The more specific objectives of the NLSCY-North are:

(i) To determine the prevalence of various biological, social and economic characteristics and risk factors and life experiences of children and youth in Canada;

(ii) To monitor the impact of such risk factors, life events and protective factors on the development of these children;

(iii) To provide this information to policy and program officials for use in developing effective policies and strategies to help children and youth people live healthy, active and rewarding lives.

5

4.2. Sample

The primary sampling unit in NLSCY-North was a household. A simple random sample was selected from a list of addresses in each community with the exception of two strata in the Yukon where random phone numbers were used for sampling. The randomly selected families with at least one child aged 0 to 11 years were eligible to be included in the NLSCY-North. The NLSCY-North sample for cycle 1 was constructed to guarantee that the sample size is big enough to be stratified by seven age groups, 0-11 months, 1, 2-3, 4-5, 6-7, 8-9, 10-11 years.

The populations from Indian reserves, Canadian armed force bases and institutions were excluded from the target population (12.7% of children aged 0 to 11 in Yukon and 6.2% of children aged 0 to 11 in the Northwest Territories).

4.3. Sample size

The cycle 1 of NLSCY-North was comprised of 1,059 children from the Yukon, of 573 children from Northwest Territory and of 772 children from Nunavut which ended up to a total of 2,404 children.

4.4. Data collection:

Data was collected using paper questionnaires from September 1994 to April 1995. Several questionnaires, which were administered in the survey, are described below:

A. Household questionnaire: It covered basic demographic information for each household member, dwelling conditions and household income. A person was assigned as Person Most Knowledgeable (PMK) about child. The PMK was

asked to complete two questionnaires: the parent questionnaire and the child questionnaire.

B. Parent questionnaire: It was designed to collect information about the PMK and his or her spouse. The information included education, labor force, and income.

C. Child questionnaire: a maximum of three children could be randomly selected from one household. The topic in the questionnaire included health, behavior, education, parenting and custody history.

4.5. Interviewing

Specially trained persons were hired to conduct the interviews by phone or in person.

4.6. Non-response

In order to increase the response rate, the individuals who refused to answer the questionnaire at the first visit or call were re-visited by a senior or a second call by the interviewer.

4.7. Sample weighting:

As recommended by Statistics Canada, a "sample" weight was used in all statistical analysis in this study. This weight was obtained by multiplying the population weight by the sample size (2,404) and divided by the total population, which is the target population in our study. This produces a mean weight of 1 and a sum of weights equal to the sample size. The advantage of this adjustment is that an over-estimation of the significance (false positive) is avoided while maintaining the

same distributions as those obtained when using the population weight.

The calculation of weights for children depended on the sampling frame from which they were selected. Because of some differences in the sampling frames between Yukon and Northwest Territories, the weighting calculation was also different. Sample weighs were used in the cross-sectional study analysis and longitudinal weights were used in the incidence rate study.

4.8. Variables and definitions used in this study

4.8.1 Variable list

NLSCY-North covers very broad information in the questionnaires. The factors used in this study were selected at three levels, the child, parental and household level, as shown below.

Child level predictors included age, sex, place of birth, maternal smoking during pregnancy, maternal drinking during pregnancy, gestational age, birth weight, prenatal problems, breast-feeding, height, weight, obesity, language spoken at home, children temperament, physical activeness, twin sibling, daycare attendance and child's allergy.

Parental level predictors included marital status, mother's current age and age at child's birth, parents' education, total income, socio-economic status, place of birth, immigrant status, smoking habit, drinking habit, allergy history, past history of asthma, asthma in the last 12 months and wheezing in the last 12 months.

Household predictors included number of children less than 17 years, number of occupants, number of bedroom, dwelling type, dwelling condition, dwelling ownership and location of home.

4.8.2 Asthma related questions in the questionnaire:

- *Ever asthma*: "Has the child ever had asthma that was diagnosed by a health professional?"
- *Wheezing cases*: "Has he/she had wheezing in the chest at anytime in the last 12 months?
- *Current wheezing*: excluding asthma ever cases from wheezing
- *Current asthma*: "Has he had an attack of asthma in the last 12 months?"
- *Asthma incidence cases*: Children without asthma in the cycle 1 who have been followed-up more than one cycle, and reported asthma in either cycle 2 and/or cycle 3.
- *Wheeze incidence cases*: Children without wheeze in the cycle 1 who were followed-up more than one cycle, and reported wheeze in either cycle 2 and/or cycle 3.

4.9. Statistics methods:

4.9.1 Cross-sectional analysis

The prevalence of asthma and wheezing in the Aboriginal and non-Aboriginal samples, as well as different demographic characteristic specific prevalence of asthma and wheezing, were calculated with 95% confidence intervals (95% CI). Logistic regression with generalized estimating equations (GEE) techniques (Dupont, 2002) to adjust for clustering of children from the same family were used to determine significant factors associated with asthma and wheezing in Aboriginal and non-Aboriginal children. Normalized cross-sectional weights were applied in the cross-sectional analysis. All factors that were significant at 20% level were considered for the multivariate analysis. A purposeful-selection method was used to determine

important factors in the multivariate logistic regression. Mantel-Haenszel stratified analysis was also used to determine effect modification or confounding of important associated factors between Aboriginal and non-Aboriginal children.

In order to study the factors associated with prevalence of asthma and wheezing in aboriginal and non-aboriginal children respectively, an interaction term between race and each of the significant factors was introduced into multivariate model.

4.9.2 Longitudinal analysis

Incidence rates of wheeze and asthma were determined using the follow-up data of the children without a history of asthma and/or wheeze at the baseline sampling. Incidence rate ratios (IRR) and p-values were calculated in Poisson regression model. Normalized longitudinal weights were used to calculate incidence rate of asthma and wheezing. Person-years were calculated using the follow-up time for each child. Each potential factor was considered in the Poisson regression model individually to identify factors associated with asthma incidence rate at a univariate level. All factors that were significant at 20% level were considered for the multivariate analysis. Clinically important risk factors including child's age, child's sex, child's racial status, child's allergy history, residence of territory, maternal asthma history and maternal smoking habit were forced into the multivariate model.

4.9.3 Purposeful selection methods

- Building the main effects model

Step 1: A univariate logistic regression was fitted to each independent variable.

Step 2: All variables, which were significant at 20% level and/or clinically important, were selected for the multivariate model.

Step 3: A multi-variable model was developed.

Step 4: All variables in the multivariate model, which were significant at the 5% level, were included.

Step 5: A reduced multi-variable model was developed and the likelihood test was performed.

Step 6: Any confounders whose parameter changed by more than 15% due to the inclusion of another independent variable were identified.

Step 7: A reduced multi-variable model including all confounders was developed.

Step 8: The model variables were tested for linear assumption.

- Selecting interaction effects.

Step 9: A multivariate model was developed with one interaction item added at a time

Step 10: All interaction items, which were significant at the 5% level in the multivariate model, were identified.

Step 11: A final model including main effects and significant interactions was developed.

4.10 Identification of asthma and wheezing related literatures:

Several methods were used to identify asthma and wheezing related research papers. Firstly, the relevant papers were identified in Pubmed and MEDLINE using the key words asthma, wheezing, birth cohort, aboriginal children, first nation, native children. Secondly, in order to find reports and published papers, which are not usually covered in Pubmed and MEDLINE, a search was also carried out using GOOGLE search engine and government websites were searched for asthma and wheeze related papers. Finally, additional literature was identified through personal communication with asthma epidemiologists and specialists.

Chapter 5

Results

5.1. Descriptive results

In this section, distributions of different demographic characteristics of the NLSCY-North are given from Table 1 to Table 8.

The Primary Sampling Union (PSU) of this survey was a household and the observation unit was child. A total of 2,404 children were chosen from 1,384 households in the three territories. In the NLSCY-North, a maximum of three children was chosen from one household. The distribution of households by number of children chosen is given in Table 1. Two or more children from a single household were chosen from 54.6% of the households.

Age distributions of children in the Yukon, Nunavut and Northwest Territories are shown in Table 2. In each age group, a majority of the children was chosen from Northwest Territory, which was followed by Yukon and Nunavut Territories.

Of the 2,345 children, 1,399 (59.7%) were of Aboriginal ancestry. As shown in Table 3, racial distributions between the three Territories were significantly different (χ^2=696.1, df=2, p<0.001). Nunavut Territory had the highest proportion of Aboriginal children.

Table 4 reveals that the gender distribution was very similar in the three Territories (χ^2=0.22, df =2, p=0.90). As shown in Table 5, gender distribution was very similar in infants and toddlers (0 to < 2 years), pre-school children (3 to < 5 years) and school-age children (5 to < 12 years). The gender differences were not statistically significant (χ^2=0.11, df =2, p=0.95). As shown in Table 6, the racial distribution was quite similar in the three age groups (χ^2=0.33, df =2, p=0.84).

As shown in Table 7, the racial distribution was very similar in females and males with approximately 60% of Aboriginal children among females and males respectively (χ^2=0.06, df =1, p=0.94).

As shown in Table 8, age distribution was similar among males and females in Aboriginal and non-Aboriginal children. The differences in age distribution between male and females were not statistically significant in Aboriginal children (χ^2=0.92, df =2, p=0.63), and in non-Aboriginal children (χ^2=0.79, df=2, p=0.67).

Table 1. Distribution of households by number of children.

Number of Children	Number of households (%)
1	628 (45.4)
2	492 (35.5)
3	264 (19.1)
Total	1,384 (100.0)

Table 2. Age distributions of children in the three territories (N=2,404).*

Age	Yukon (%)	Northwest (%)	Nunavut (%)
0	21.8	40.7	37.6
1	25.0	41.3	33.8
2	25.8	40.1	34.1
3	25.1	41.0	33.8
4	23.9	41.1	35.0
5	24.2	39.9	35.9
6	23.9	42.0	34.1
7	24.6	42.4	33.0
8	25.9	40.9	33.2
9	28.1)	39.9	32.1
10	28.3	41.1	30.6
11	28.8	39.5	31.7
Total	25.4	40.8	33.8

* Normalized weights were applied in calculating the proportions.

Table 3. Racial distributions of children in the three territories (N=2,345).* †

	Yukon (%)	Northwest (%)	Nunavut (%)
Aboriginal	22.3	56.2	91.8
Non-aboriginal	77.7	43.8	8.2
Total	100	100	100

* Normalized weights were applied; † 59 children had missing values for race.

Table 4. Gender distributions of children in the three territories (N=2,404).*

	Yukon (%)	Northwest (%)	Nunavut (%)
Females	47.5	48.7	48.4
Males	52.5	51.3	51.6
Total	100	100	100

* Normalized weights were applied.

Table 5. Distributions of children by age and gender (N=2,404).*

	Infant/toddlers (%)	Pre-school (%)	School-age (%)	Total (%)
Females	48.6	48.4	47.9	48.2
Males	51.4	51.6	52.1	51.8
Total	100	100	100	100

* Normalized weights were applied.

Table 6. Distributions of children by race and age groups (N=2,345).* †

	Infant/toddlers (%)	Pre-school (%)	School-age (%)	Total (%)
Aboriginal	60.6	59.8	59.1	59.7
Non-aboriginal	39.4	40.2	40.9	40.3
Total	100	100	100	100

* Normalized weights; † 59 children had missing values for race.

Table 7. Distributions of children by race and gender (N=2,345).* †

	Females (%)	Males (%)	Total (%)
Aboriginal	59.7	59.6	59.7
Non-aboriginal	40.3	40.4	40.3
Total	100	100	100

* Normalized weights were applied; † 59 children had missing values for race.

Table 8. Distributions of children by race, age and gender (N=2,345).* †

	Aboriginal females (%)	Aboriginal males (%)	Non-aboriginal females (%)	Non-aboriginal males (%)
Infants and toddlers	25.8	26.0	25.5	24.4
Pre-school	28.3	26.0	25.7	28.3
School-age	45.9	48.0	48.8	47.3
Total	100	100	100	100

* Normalized weights were applied; † 59 children had missing values for race.

5.2. Asthma and wheeze prevalence

As shown in Figure 1, among the three Territories, the Northwest Territory (NWT) had the highest prevalence of *ever-asthma* (8.80%; 95% CI: 7.0-10.6); however, the differences between the three Territories were not statistically significant (χ^2=3.2, df =2, p=0.21). The NWT also had the highest prevalence of *current-asthma* (5.49%; 95% CI: 4.1-6.9), which was significantly higher than the other Territories (χ^2=17.6, df =2, p<0.001). Nunavut had the highest prevalence of *current-wheeze* (11.97%; 95% CI: 9.7-14.2), which was significantly higher than the other Territories (χ^2=4.1, df =2, p=0.13).

As shown in Figure 2, school-age children had the highest prevalence of ever-asthma (8.80%; 95% CI= 7.2-10.5). The differences between three age groups were not statistically significant (χ^2=4.5, df =2, p=0.10). Infants and toddlers had slightly higher prevalence of *current-asthma* (3.72%; 95% CI: 2.2-5.2), and greater prevalence of *current-wheeze* (18.9%, 95%CI: 15.9-22.0). Only the differences in prevalence of *current-wheeze* were statistically significant between the three age groups (*current-asthma*: χ^2=0.02, df=2, p=0.99; *current-wheeze*: χ^2=72.9, df=2, p<0.001).

As shown in Figure 3, prevalence of *ever-asthma* and *current-asthma* were significantly greater in non-Aboriginal children than in Aboriginal children (*ever-asthma*: 10% vs 5.7%, χ^2=15.5, df =1, p<0.001; *current-asthma*: 5.3% vs 2.4%, χ^2=14.0, df =1, p<0.001). This was reversed for prevalence of *current-wheeze* with Aboriginal children having significantly higher prevalence than non-Aboriginal children (11.5% vs 8.1%, χ^2=7.12, df =1, p=0.008).

As shown in Figure 4, prevalence of *ever-asthma* was similar between boys and girls (χ^2=0.01, df =1, p=0.92). Prevalence of *current-asthma* and *current-wheeze*

were slightly higher in boys than girls; however, but the differences weren't statistically significant (*current-asthma*: χ^2=0.75, df =1, p=0.38; *current-wheeze*: χ^2=0.60, df =1, p=0.44).

Age and race specific prevalence of ever-asthma is illustrated in Figure 5. There were no differences in prevalence between Aboriginal and non-Aboriginal infants and toddlers (6.4% vs 6.3%). In pre-school and school-age children, prevalence of *ever-asthma* was higher in non-Aboriginal children than in Aboriginal children (pre-school: 8.8% vs 5.7%; school-age: 12.6% vs 5.2%). The difference was statistically significant only in school-age children (infants & toddlers: χ^2=0.00, df =1, p=0.99; pre-school: χ^2=2.24, df =1, p=0.13; school-age: χ^2=19.9, df =1, p<0.001).

Age and race specific prevalence of *current-asthma* are illustrated in Figure 6. The prevalence of *current-asthma* was greater in non-Aboriginal children than in Aboriginal children in all age groups (infants/toddlers: 4.5% vs 3.51%; pre-school: 5.0% vs. 2.7%; school-age: 5.9% vs 1.5%). These differences were only significant in the school-age children (infants/toddlers: χ^2=0.34, df =1, p=0.56; pre-school: χ^2=2.31, df =1, p=0.13; school-age: χ^2=16.0, df =1, p<0.001).

The age and race specific prevalence of *current-wheeze* is illustrated in Figure 7. The prevalence of *current-wheeze* in infants and toddlers was higher in Aboriginal children than in non-Aboriginal children (22.04% vs 12.07%) and the difference was statistically significant (χ^2=9.52, df=1, p=0.002). While the prevalence in other age groups was higher in Aboriginal than non-Aboriginal children (pre-school: 10.0% vs 9.8%; school-age: 6.6% vs 5.2%), the differences were not statistically significant (pre-school: χ^2=0.01, df =1, p=0.93; school-age: χ^2=0.99, df =1, p=0.42).

In the three age groups, as shown in Figure 8.1, prevalence of *current-wheeze* was higher in Aboriginal than non-Aboriginal children for both girls and boys in

infants and toddlers and school-age children. The difference, however, was only significant in infant and toddler males (χ^2=9.5, df =1, p=0.002).

As shown in Figure 8.2, school-age males and females, and males in pre-school age and under had significantly higher prevalence of *ever-asthma* in non-Aboriginal than in Aboriginal children (girls in school-age: χ^2=4.9, df =1, p=0.03; boys in school-age: χ^2=16.4, df =1, p<0.001; boys under pre-school age: χ^2=5.4, df =1, p=0.02). In infants and toddlers, the prevalence of *ever-asthma* was higher in Aboriginal than in non-Aboriginal girls; however, the difference was not statistically significant (χ^2=0.96, df=1, p=0.33).

Figure 1 Prevalence of ever-asthma, current-asthma and current-wheeze by the three territories

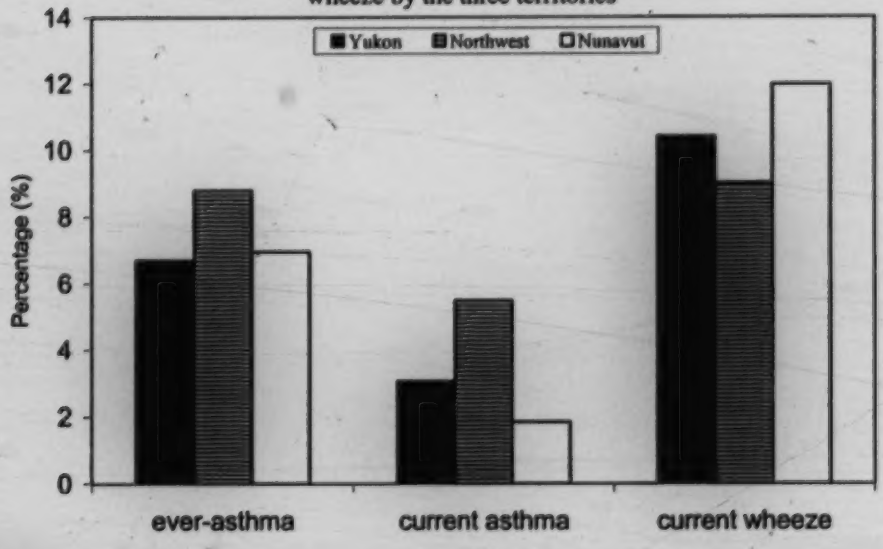


Figure 2 Prevalence of ever-asthma, current-asthma and current-wheeze in the three age groups

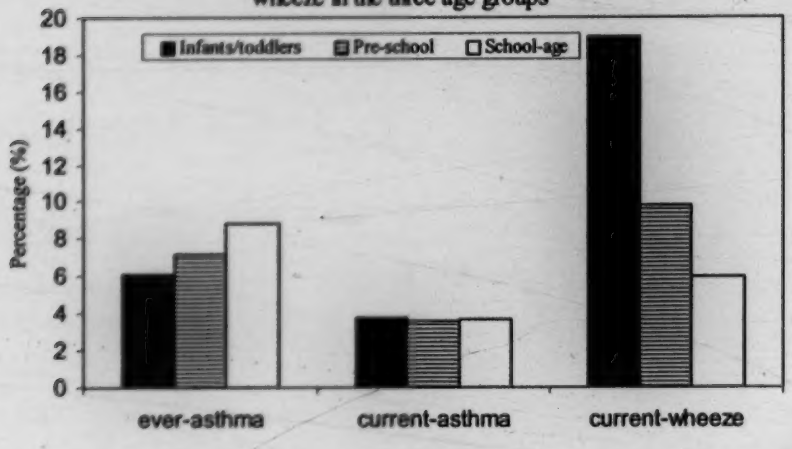


Figure 3 Prevalence of ever-asthma, current-asthma and current-wheeze by race

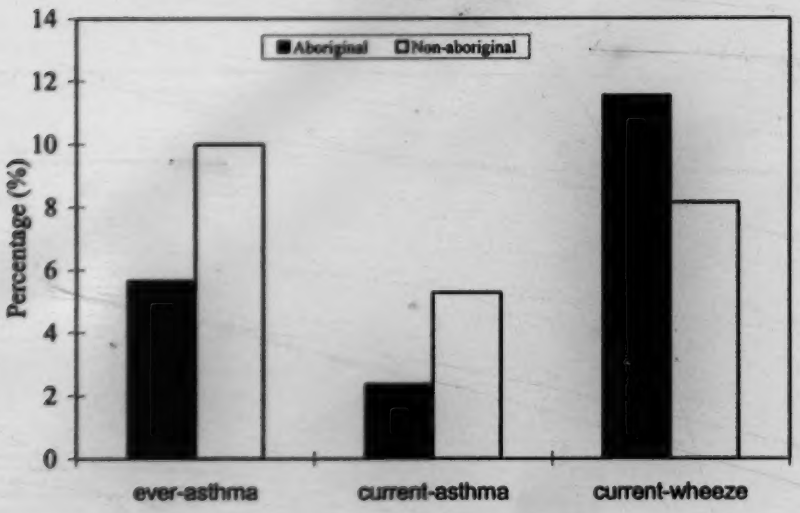


Figure 4 Prevalence of ever-asthma, current-asthma and current-wheeze by gender

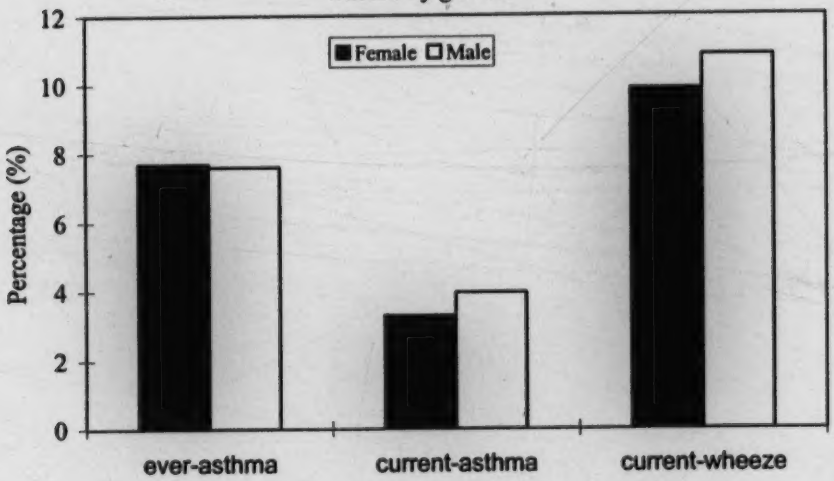


Figure 5 Prevalence of ever-asthma by race and age groups

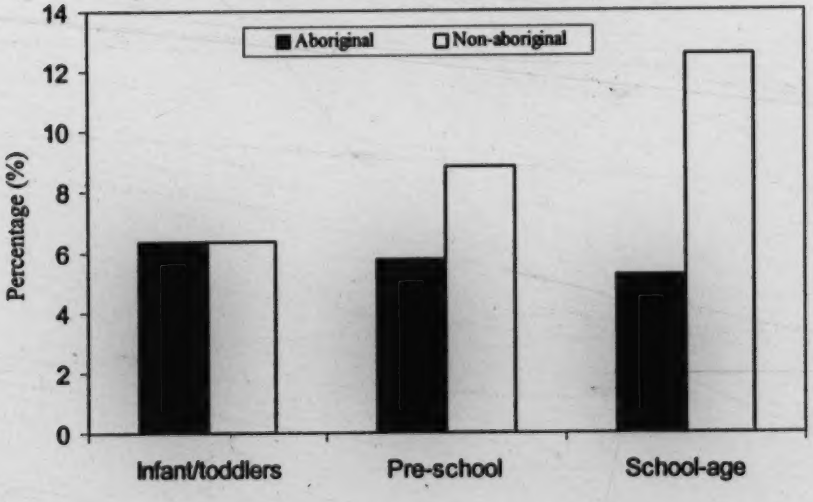


Figure 6. Prevalence of current-asthma by race and age groups

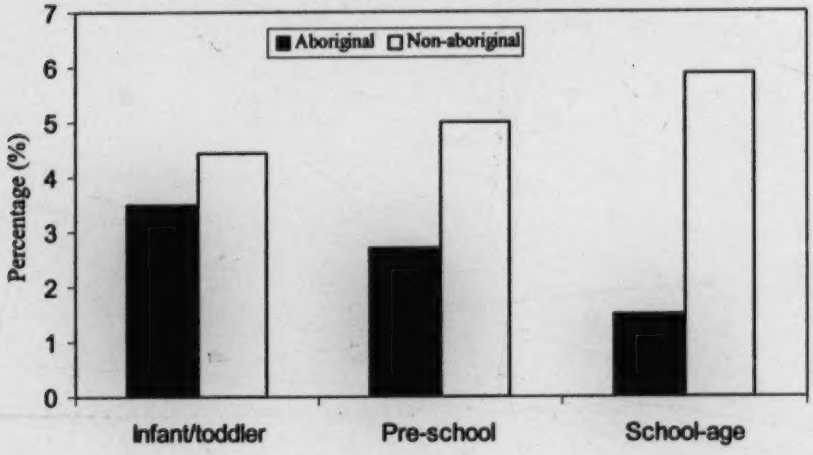


Figure 7. Prevalence of current-wheeze by race and age

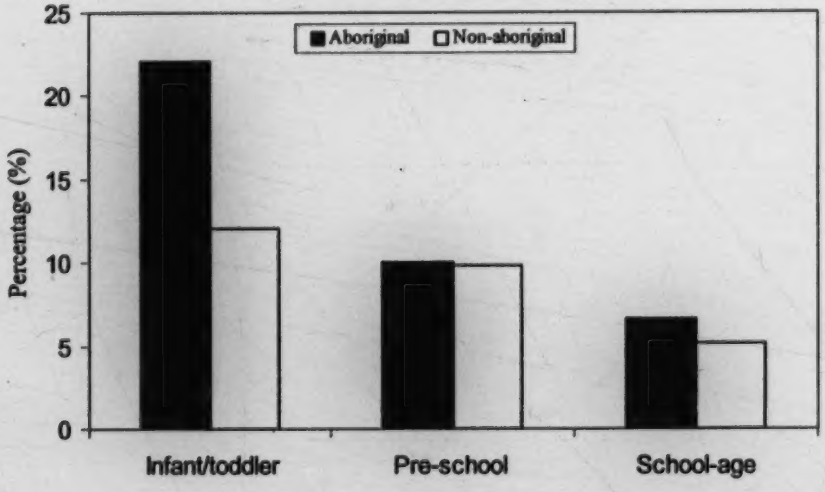


Figure 8.1 Prevalence of current wheeze by race age and gender

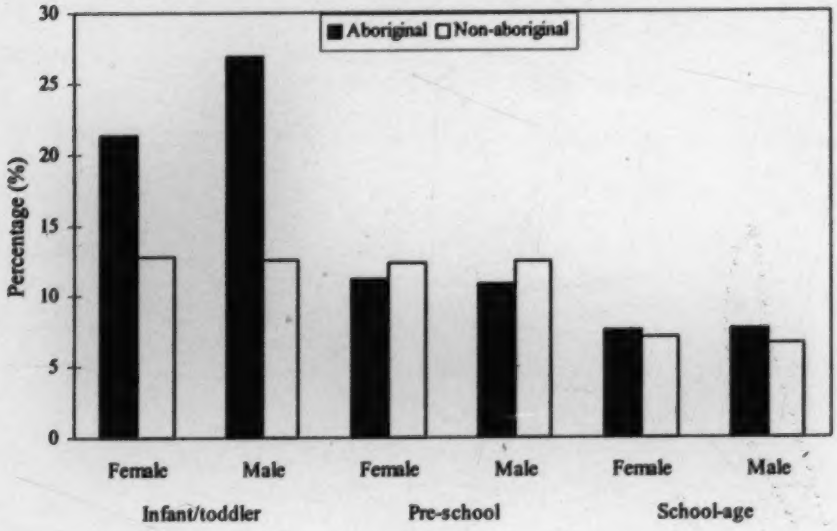
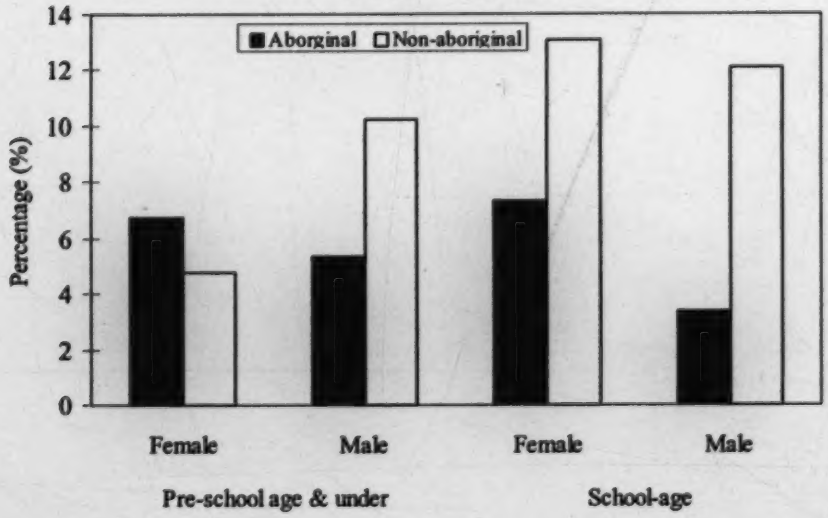


Figure 8.2 Prevalence of ever-asthma by race, age and gender



5.3. Factors associated with asthma and wheeze prevalence

In this section, factors associated with the prevalence of *ever-asthma* and *current-wheeze* are reported using multivariate logistic regression analysis.

5.3.1 Risk factors of prevalence of ever-asthma

The univariate results from the logistic regression to identify factors associated with the prevalence of *ever-asthma* are provided in Table 9. These factors associated with *ever-asthma* were race, child's allergic history, mother's education level, region, biological mother's allergy, biological mother's asthma, and biological mother's wheeze in last 12 months and mother's drinking habit.

Effect modifiers were identified if the interaction term of one of the variables with race was statistically significant at 5% level. Those variables whose interaction terms were not statistically significant, however their model inclusion resulted in a change of the race parameter of > 20%, were considered confounder variables. As shown in Table 10, three effect-modifiers and three confounders were identified using this method.

The factors associated with *ever-asthma* which were significant at $p<0.20$ were included in the multivariate analysis. As shown in Table 11, after having introduced all clinically important factors, effect-modifiers and confounders into the model, we identified the following four significant variables: the child's allergy history (OR = 6.37; 95% CI: 3.78-10.72), the biological mother's asthma history (OR = 1.94; 95% CI: 1.01-3.70), dwelling ownership (OR = 1.77; 95% CI: 1.06-2.96) and territory of residence (OR = 0.39; 95% CI: 0.17-0.89).

A stratified analysis was conducted to explore the factors associated with *ever-asthma* between Aboriginal and non-Aboriginal children. As shown in Table 12,

three significant factors were associated with the prevalence of *ever-asthma* in Aboriginal children were: the child's allergic history (OR = 6.64; 95% CI: 2.77-15.94), the biological mother's ever-asthma (OR = 3.73; 95% CI: 1.24-11.21) and territory of residence (OR = 3.91; 95% CI: 1.49-10.27). Three significant factors associated with the prevalence of *ever-asthma* in non-Aboriginal children were the child's allergic history (OR = 6.20; 95% CI: 3.21-11.97), dwelling ownership (OR = 1.97; 95% CI: 1.03-3.79) and territory of residence (OR = 1.96; 95% CI: 1.05-3.70).

5.3.2 Factors associated with the prevalence of current-wheeze

Using the method described in section 5.3.1, factors significantly associated with the prevalence of *current-wheeze* were: age, race, number of children in the house, number of older siblings, region, biological mother's asthma and mother's smoking/drinking habit (Table 13). Using the method described in the previous section, one effect-modifier and two confounders were identified for the prevalence of *current-wheeze* (Table 14).

As shown in Table 15, after introducing all clinically important and statistically significant factors, the effect-modifier and confounders into the regression model, we identified the following four significant factors: infants and toddlers (OR = 2.44; 95% CI: 1.53-3.88), child physical activity (OR = 0.36; 95% CI: 0.16-0.81), number of older siblings (OR = 0.58; 95% CI: 0.35-0.94) and mother's smoking history (OR = 1.77; 95% CI: 1.10-2.85).

A stratified analysis was conducted for Aboriginal and non-Aboriginal children. As shown Table 16, three factors associated with the prevalence of *current-wheeze* in Aboriginal children were identified: infants and toddlers (OR = 2.70; 95% CI: 1.47-4.94), less physical activity (OR = 2.61; 95% CI: 0.95-7.17) and mother's daily

smoking (OR = 1.91; 95% CI: 0.98-3.71). Infants and toddlers were an age group significantly associated with the prevalence of *current-wheeze* in non-Aboriginal children (OR = 2.09; 95% CI: 1.04-4.20), whereas the number of older siblings appears protective (OR = 0.46; 95% CI: 0.22-0.95).

5.3.3 Confounding effects of mother smoking habit in the prevalence of current-wheeze

As shown in Table 14, the mother's smoking habit was a strong confounder that led to more than 43% change in the parameter of race when included in the logistic regression. Further analysis was conducted to elucidate the confounding effect of mother's smoking habit on the association between prevalence of *current-wheeze* and other significant risk factors. As shown in Table 17, among infants and toddlers, as long as a child's mother was a daily smoker, the odds ratios were statistically significant regardless the differences in race and number of older sibling. Therefore, mother's smoking habit could explain the observed differences in race and number of older siblings in infants and toddlers.

Table 9. Univariate analyses for risk factors of *ever-asthma* prevalence.*

		OR	95% CI	p-values†
Sex	Male	1.0		
	Female	0.92	0.66-1.31	0.66
Age	School-age	1.0		
	Pre-school	0.84	0.56-1.25	0.22
	Infant/toddler	0.75	0.47-1.18	
Race	Non-Aboriginal	1.0		
	Aboriginal	0.56	0.37-0.83	0.01
Territory of residence	Northwest	1.0		
	Yukon+Nunavut	0.77	0.51-1.16	0.21
Child's allergy	No	1.0		
	Yes	12.97	4.03-10.42	< 0.01
Biological parent status	No	1.0		
	Both	2.08	0.93-4.66	0.18
	One	2.16	0.92-5.10	
Mother's Educational Status	≤ Secondary	1.0		
	≥ High school	2.24	1.33-3.78	< 0.01
Region	Rural	1.0		
	Urban	1.54	1.03-2.28	0.03
Dwell in need of repairs	No	1.0		
	Yes	1.31	0.88-1.97	0.19
Biological mother's allergy	No	1.0		
	Yes	2.04	1.27-3.28	< 0.01
Biological mother's asthma	No	1.0		
	Yes	2.64	1.39-5.02	< 0.01
Biological mother's asthma in last 12 months	No	1.0		
	Yes	3.67	1.55-8.37	< 0.01
Biological mother's wheeze in last 12 months	No	1.0		
	Yes	2.28	1.01-5.14	0.05

(Table 9 continued)

		OR	95% CI	p-values†
Mother drinking habit	No	1.0		
	Yes	2.28	1.01-5.14	0.05
Mother's place of birth	Asia and other	1.0		
	Canada	1.90	0.40-9.14	0.20
	US & Europe	0.86	0.11-6.65	
Household income	≥ 40,000	1.0		
	≤ 14,999	0.59	0.33-1.05	0.16
	15,000-39,999	0.77	0.48-1.25	

* Normalized weights were applied; † p-values are from the Wald's test for dichotomous variable and Type III –chi square test for tri-chotomous variable.

Table 10. Effect modifiers, confounders of race for *ever-asthma.*

	Effect modifier	Confounder	
	Interaction with Race	Parameter Estimates of Race	Change in parameter of race
Race		-0.59	
Child's allergy	NS	-0.41	29.73%
Mother's education status	SG		
Dwelling ownership	SG		
Region	SG		
Mother's smoking habit	NS	-0.74	26.30%
Mother martial status	NS	-0.63	7.07%
Child language	NS	-0.45	22.73%
House hold income	NS	0.52	12.24%

NS Not significant at p=0.05; SG Significant at p=0.05.

Table 11. Multivariate analyses for prevalence of *ever-asthma.*

		OR	95% CI
Child's allergy	No	1.0	
	Yes	6.37	3.78-10.72
Biological mother's allergy	No	1.0	
	Yes	1.94	1.01-3.70
Territory of residence	NWT	1.0	
	Yukon + Nunavut	0.39	0.17-0.89
Dwelling ownership	Yes	1.0	
	No	1.77	1.06-2.96

Table 12. Stratification by race in the multivariate logistic regression (N=1,805).

		Aboriginal children		Non-aboriginal children	
		OR	95%CI	OR	95%CI
Territory of residence					
	Northwest	1.00		1.00	
	Nunavut	3.91	1.49-10.27	1.34	0.36-5.02
	Yukon	0.58	0.23-1.45	1.96	1.05-3.70
Child's allergic history	No	1.00		1.00	
	Yes	6.64	2.77-15.94	6.20	3.21-11.97
Biological mother's ever-asthma	No	1.00		1.00	
	Yes	3.73	1.24-11.21	1.50	0.73-3.11
Dwelling ownership	Yes	1.00		1.00	
	No	1.44	0.69-3.02	1.97	1.03-3.79

Table 13. Univariate analysis for risk factors of prevalence of *current wheeze.**

		OR	95% CI	p-values†
Age	School-age	1.00		
	Pre-school	1.64	1.12-2.41	0.01
	Infant/toddler	3.86	2.71-5.49	
Race	Non-aboriginal	1.0		
	Aboriginal	1.47	1.05-2.06	0.03
Number of children in the house	1	1.0		
	0	1.95	1.25-3.02	0.01
	2+	1.03	0.70-1.54	
Number of older siblings	1	1.0		
	0	0.50	0.32-0.79	< 0.01
	2+	1.09	0.75-1.62	
Region	Rural	1.0		
	Urban	0.78	0.56-1.09	0.14
Biological mother's asthma	No	1.0		
	Yes	0.54	0.26-1.12	0.09
Biological mother's wheeze in last 12 months	No	1.0		
	Yes	0.58	0.24-1.39	0.23
Mother's smoking habit	Daily	1.0		
	Never	0.52	0.36-0.75	0.01
	Occasionally	0.70	0.42-1.19	
Mother's smoking dose	21+	1.00		
	0-10	0.47	0.30-0.75	< 0.01
	11-20	0.86	0.53-1.42	
Mother's drinking habit	No	1.00		
	Yes	1.41	0.94-2.14	0.01
Mother's food allergy	No	1.00		
	Yes	1.08	0.50-2.31	0.87

(Table 13 continued)

		OR	95% CI	p-values†
Household income	≥ 40,000	1.00		
	≤ 14,000	1.32	0.88-1.96	0.14
	15,000 – 39,999	1.45	1.00-2.12	
Child physical activity	Less	1.00		
	More	0.79	0.37-1.66	0.07
	Equal	0.55	0.26-1.15	
Marital Status	Widow	1.00		
	Married	1.01	0.60-1.72	0.17
	Single	1.61	0.82-3.18	

* Normalized weights were applied; † p-values are from the Wald's test for dichotomous variable and Type III –chi square test for tri-chotomous variable

Table 14. Effect modifiers, confounders of race for prevalence of *current wheeze.*

	Effect modifier	Confounder	
	Interaction with Race	Parameter of race	Change in parameter of race
Race		0.3840	
Territory of residence	NS	0.4232	10.21%
Region	SG		
Mother's smoking habit	NS	0.2177	43.31%
House hold income	NG	0.2848	25.83%

NS Not significant at p=0.05; SG Significant at p=0.05.

Table 15. Multivariate analyses for the prevalence of *current wheeze* (N=1,537).

		OR	95%CI
Age	≥ Pre-school	1.0	
	Infants/toddlers	2.44	1.53-3.88
Child physical Activity	Less	1.0	
	More	0.56	0.25-1.28
	Equal	0.36	0.16-0.81
Number of older siblings	1	1.0	
	0	0.58	0.35-0.94
	2+	0.69	0.42-1.14
Mother's smoking habits	Never or Occasional	1.0	
	Daily	1.77	1.10-2.85

Table 16. Stratification by race in multivariate analysis for *current wheeze* (N=1,537).

		Aboriginal		Non-aboriginal	
		OR	95%CI	OR	95%CI
Age	≥ Pre-school	1.0			
	Infant/toddler	2.70	1.47-4.94	2.09	1.04-4.20
Child physical activity	More & Equal	1.0			
	Less	2.61	0.95-7.17	1.72	0.54-5.47
Mother's smoking habit	Never/ Occasional	1.0			
	Daily	1.91	0.98-3.71	1.36	0.67-2.77
Number of older siblings	1	1.0			
	0	0.67	0.35-1.28	0.46	0.22-0.95
	2+	0.61	0.35-1.04	0.90	0.36-2.23

Table 17. Confounding effects of mother smoking habit (N=1,537).

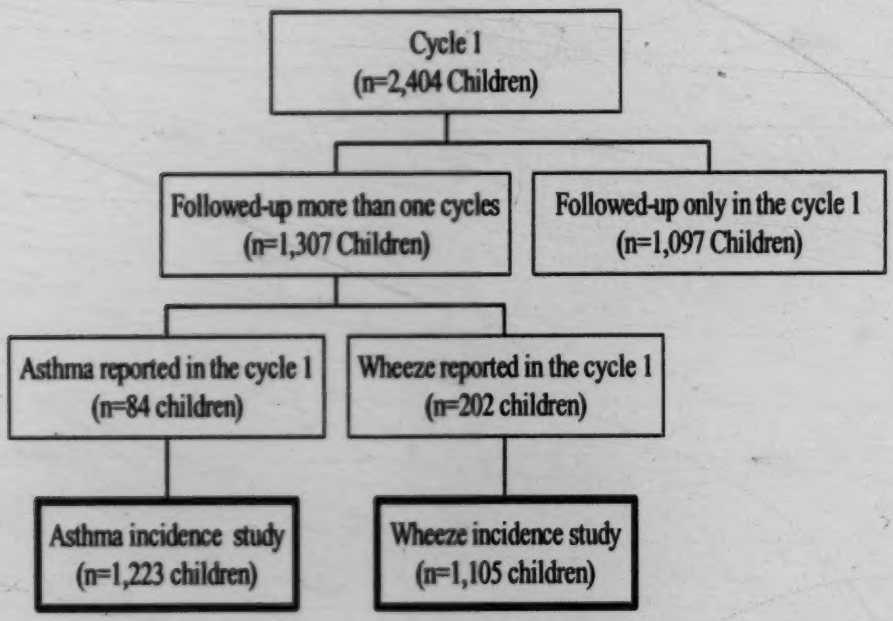
	Infants and toddlers		Pre-school and older	
	Mother smoking habit		Mother smoking habit	
	Occasionally & never	Daily	Occasionally & never	Daily
	OR	OR	OR	OR
Race				
Aboriginal	1.51	3.62*	0.92	1.60
Non-aboriginal	Reference	2.32*	Reference	1.16
N of older sibling				
0 or 1	0.59	3.40*	0.63	1.41
≥ 2	Reference	2.92*	Reference	3.20*
Physical activity				
More & Equal	Reference	4.21*	Reference	1.41
Less	4.85	4.26	1.11	3.19*

* $p < 0.05$.

5.4. Asthma and wheeze incidence rates

Of the 2,404 children who were studied in 1994-1995, 1,307 children were surveyed again in 1996-1997 and/or 1998-1999. Out of 1307 cases, 84 cases who had *asthma* in cycle 1, and 202 cases who had *wheeze* in cycle 1, were excluded from asthma and wheeze incidence studies respectively. Therefore, the sample size available for asthma and wheeze incidence studies were 1,223 and 1,105 .

Children in the incidence study



A comparison was made between demographic factors of those children who participated in only in cycle 1 with those who were followed up at cycle 2 and/or cycle 3. There were significant differences between the two groups in child's age and allergy history, biological mother's asthma history, mother's education and daily smoking, number of older siblings, total household income, and residence (Table 18).

Table 18. Comparison between those who completed more than one cycle and those who completed only the first cycle.*

			95% CI	
		Difference†	Low	High
Age	Mean (years)	0.16	0.15	0.17
Race	Aboriginal	18.6	18.59	18.67
Territory of residence	Northwest	2.0	1.92	2.00
Child allergic history	Yes	2.0	1.91	2.02
Dwelling ownership	Yes	1.2	1.20	1.28
Household income	≥ 40,000	0.6	0.58	0.66
Mother's marital status	Married	4.5	4.42	4.48
Mother's age	> 35 years	0.1	0.03	0.07
Mother allergy history	Yes	3.9	3.90	3.96
Mother asthma history	Yes	2.6	2.61	2.65
Mother drinking habit	Yes	8.2	8.11	8.19
Mother smoking habit	Daily	8.2	8.17	8.25
Mother education level	Secondary and above	6.8	6.80	6.88
Number of older siblings *	2 or more	6.9	6.84	6.92
Child physical activity	More	0.6	0.51	0.59
Child wheezing	Yes	1.0	1.01	1.09
Obesity	Yes	0.2	0.13	0.17

* Normalized weights were applied; † Difference between means or proportions.

5.4.1 Descriptive results

As shown in Figure 9, asthma and wheeze incidence rates were higher in non-Aboriginal children than in Aboriginal children, but the differences in asthma and wheeze incidence were not statistically significant.

As shown in Figure 10, asthma and wheeze incidence rates were higher in infants and toddlers than in pre-school and school-age children. The differences were not statistically significant.

Girls had higher asthma incidence rate than boys, but boys had higher wheeze incidence rate than girls (Figure 11). None of the differences was statistically significant.

As shown in Figure 12, NWT had the highest incidence rates of asthma and wheeze, and was followed by Yukon and Nunavut Territories, but the differences were not statistically significant.

As shown in Figures 13.1 and 13.2, asthma and wheeze incidence rates were higher in non-Aboriginal children than in Aboriginal children for both boys and girls. None of the differences was statistically significant.

As shown in Figures 14.1 and 14.2, asthma incidence rates were higher in non-Aboriginal children than in Aboriginal children in both Yukon/Nunavut and NWT.

As shown in Figures 15.1 and 15.2, in school-age children, asthma and wheeze incidence rates were significantly higher in non-Aboriginal children than in Aboriginal children, the differences were statistically significant (asthma: IRR=1.80, p=0.04; wheeze: IRR=1.45, p=0.05). In infants and toddlers, asthma and wheeze incidence rates were almost identical between the non-Aboriginal and the Aboriginal.

As shown in Figures 16.1 and 16.2, asthma and wheeze incidence rates were higher in non-Aboriginal children than in Aboriginal children for both boys and girls

except that asthma incidence rate was slightly lower in non-Aboriginal boys than Aboriginal boys in pre-school age and under, and that wheeze incidence rate was lower in non-Aboriginal girls than Aboriginal girls in pre-school age and under. None of differences was statistically significant.

5.4.2 Risk factors of asthma incidence rate

The results from Poisson regression models to identify risk factors of asthma incidence rate, one at time (univariate analysis), are given in Table 19. From Table 19, several risk factors of asthma incidence rate, which were significant at $p=0.05$, were sex of PMK, child allergy history, region and bio-mother's asthma history.

The risk factors which were significant at $p<0.20$ were considered in the multivariate Poisson regression model. As shown in Table 20, one risk factor which was significant at $p=0.05$, was biological mother's asthma history. Child's allergy history was almost significant ($p=0.07$).

5.4.3 Risk factors of wheeze incidence rate

Using method described in the last section, four risk factors of wheeze incidence rate as shown in Table 21, which were significant at $p=0.05$, were child's allergy history, household income, region, and biological mother's asthma history.

Using the method described in section 4.9.2, several risk factors of wheeze incidence, as shown in Table 22, which were significant at $p=0.05$, were age of child, child's allergic history, mother's education, number of older siblings, household income, territory and mother's smoking habit.

Figure 9. Asthma and wheeze incidence rates by race

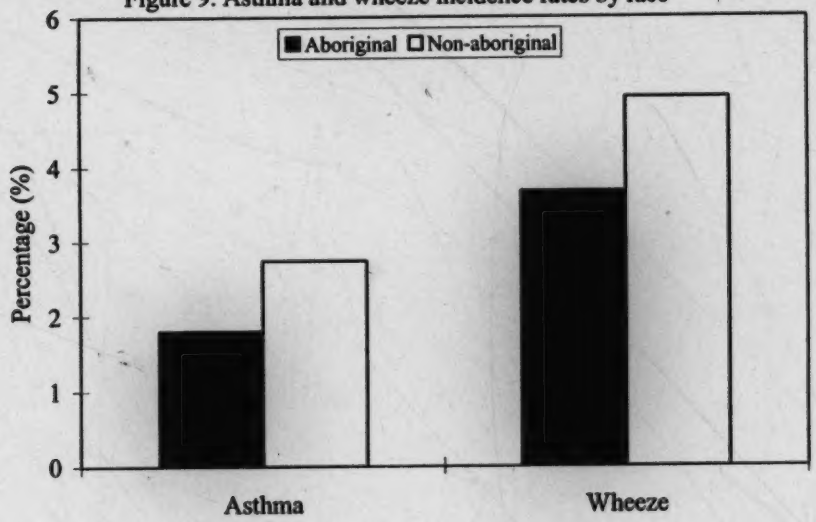


Figure 10. Asthma & wheeze incidence rates by age

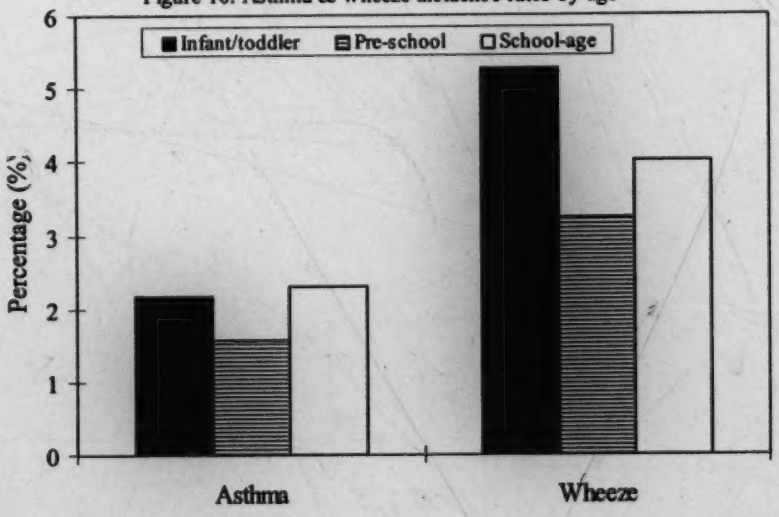


Figure 11. Asthma & wheeze incidence rates by gender

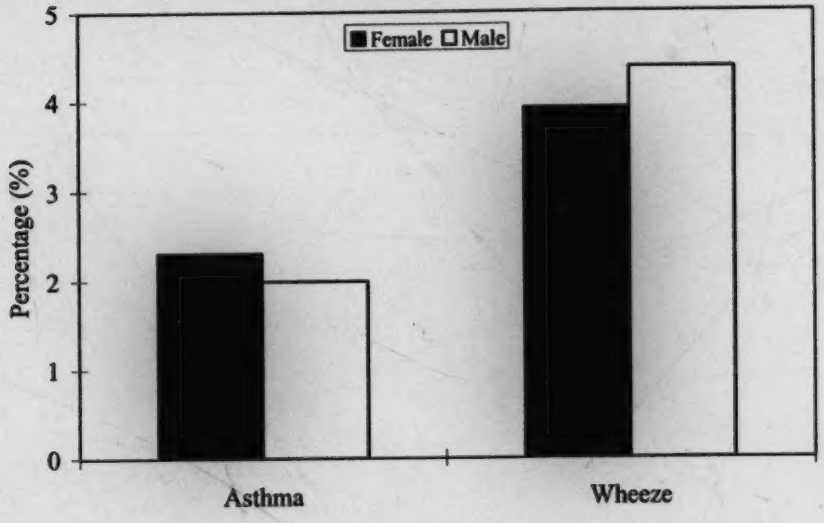


Figure 12 Asthma and wheeze incidence rates in the three territories

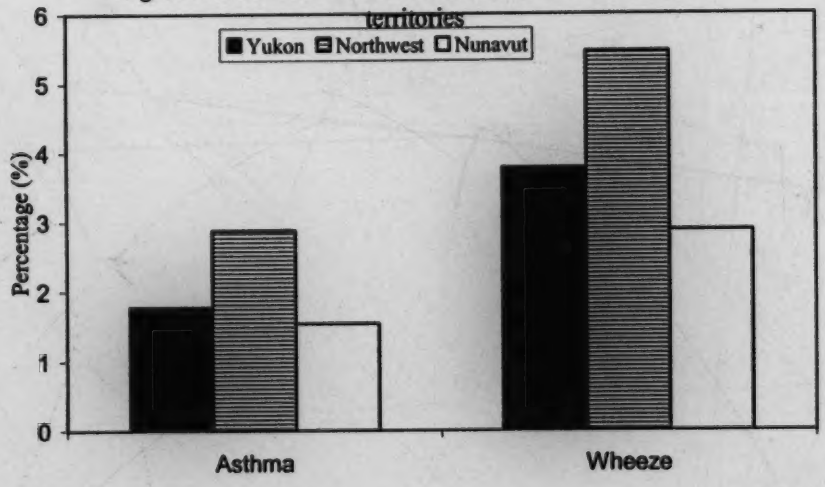


Figure 13.1 Asthma incidence rates by race & gender

Figure 13.2. Wheeze incidence rates by race and gender

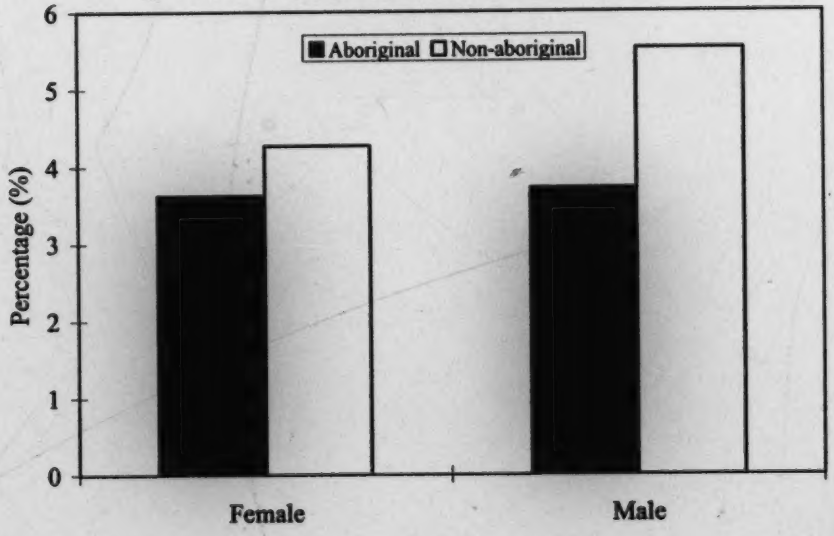


Figure 14.1 Asthma incidence rates by race & territories

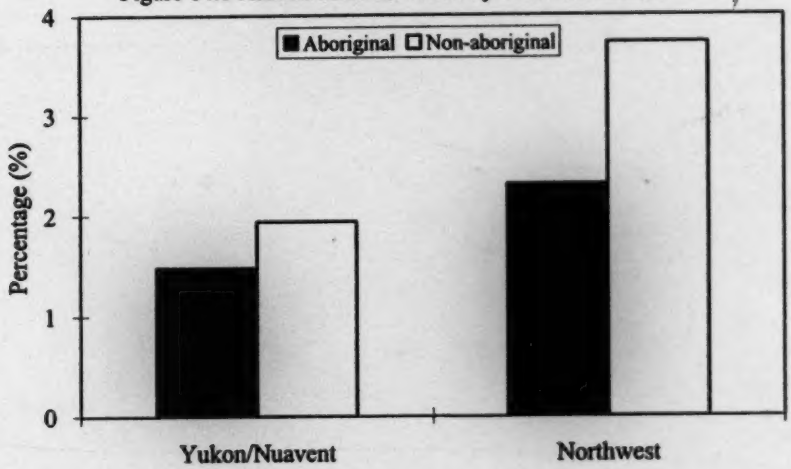


Figure 14.2 Wheeze incidence rates by race & territories

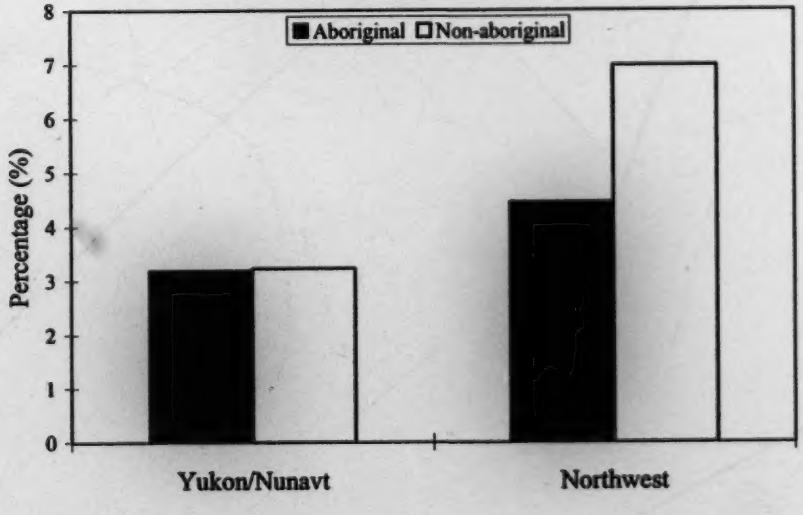


Figure 15.1 Asthma incidence rates by race and age

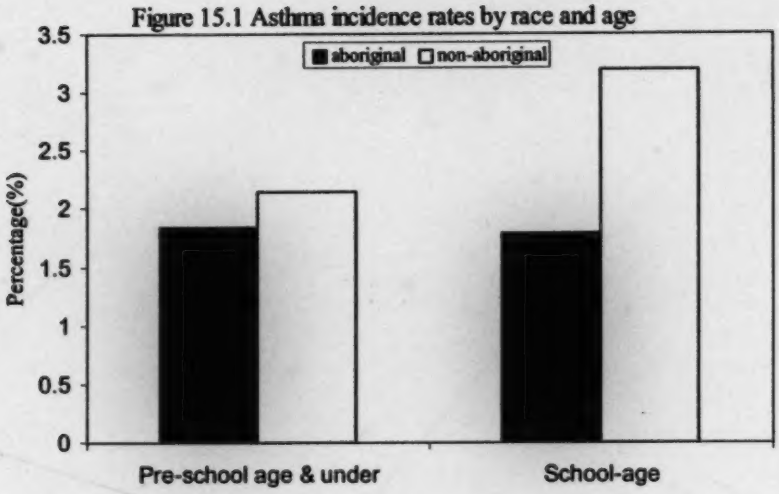


Figure 15.2 Wheeze incidence rates by race and age

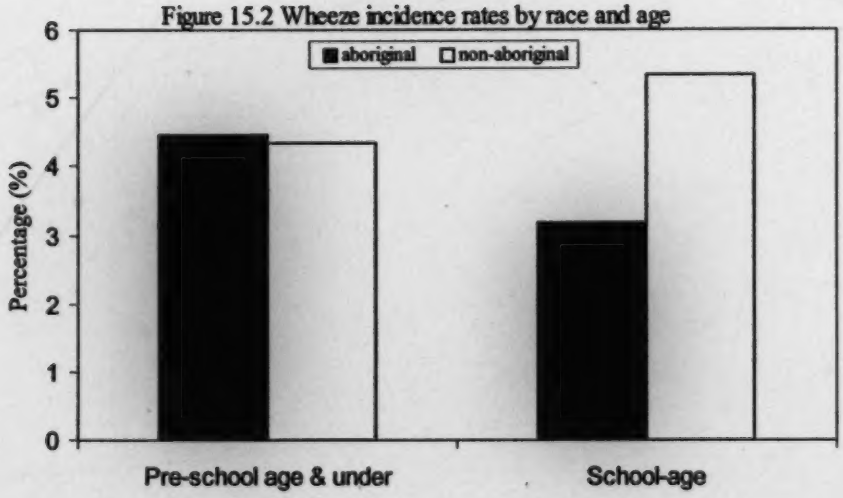


Figure 16.1 Asthma incidence rate by race,age & gender

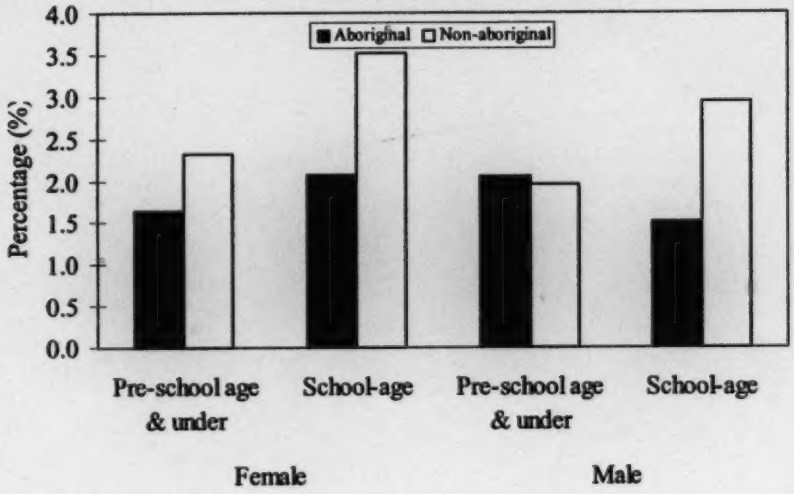


Figure 16.2 Wheeze incidence rate by race, age & gender

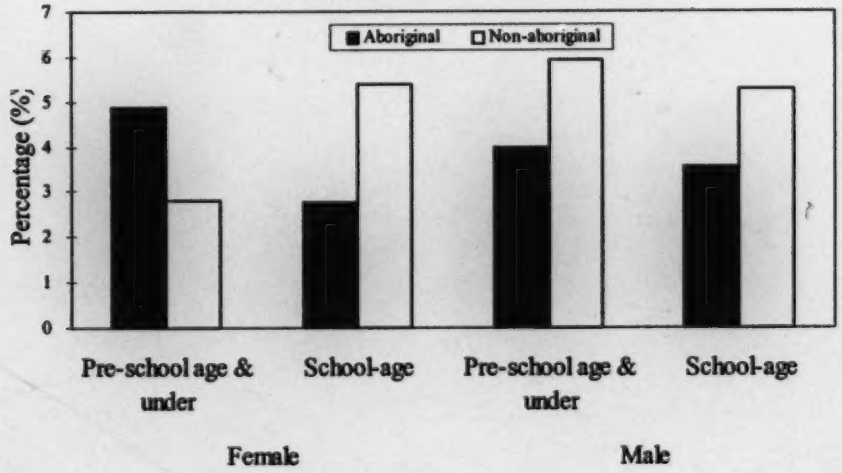


Table 19. Univariate analysis for risk factors of asthma incidence rate.*

		No of cases	Person years	Rate (%)	IRR	95% CI Low	95% CI High
Race of child	Aboriginal	54	3015.7	1.8	1		
	Non-aboriginal	47	1697.2	2.74	1.51	0.98	2.34
Age of child	Infant/toddler	25	1174.4	2.17	1		
	Pre-school	13	834.1	1.58	0.74	0.36	1.52
	School-age	64	2752.5	2.31	1.07	0.64	1.80
Sex of child	Female	53	2291.6	2.31	1		
	Male	49	2469.4	1.99	0.86	0.54	1.35
Sex of PMK	Female	77	4030.8	1.91	1		
	Male	25	730.3	3.42	1.79	1.06	3.02
Child allergy history	No	88	4365.0	2.01	1		
	Yes	12	297.8	4.13	2.0	1.05	3.85
Number of biological parents	Both	68	2930.3	2.31	1		
	One	12	772.3	1.58	0.69	0.34	1.39
	None	10	410.8	2.41	1.05	0.53	2.06
Mother education status	< Secondary	23	1268.5	1.78	1		
	Secondary	11	381.5	2.88	1.62	0.76	3.47
	High school	28	1464.0	1.9	1.07	0.57	2.01
	≥ College	26	1304.7	2.01	1.12	0.61	2.08

(Table 19. Continued)

		No of cases	Person years	Rate (%)	IRR	95% CI Low	95% CI High
Number of older siblings	None	21	1018.9	2.03	1		
	One	34	1422.2	2.36	1.17	0.61	2.22
	Two+	27	1305.6	2.09	1.04	0.53	2.02
Total household income	≤ 14,999	16	930.2	1.66	1		
	15,000 - 39,999	23	1123.3	2.08	1.25	0.65	2.42
	≥ 40,000	63	2707.5	2.34	1.4	0.79	2.50
Territory of residence	Yukon	19	1088.0	1.78	1		
	Northwest	56	1957.3	2.88	1.62	0.96	2.74
	Nunavut	26	1715.7	1.54	0.87	0.51	1.48
Region	Rural	37	2563.0	1.43	1		
	Urban	65	2198.0	2.98	2.08	1.35	3.23
Bio-mother's allergy history	No	68	3187.3	2.12	1		
	Yes	11	623.9	1.82	0.86	0.45	1.64
Bio-mother's asthma history	No	68	3647.6	1.85	1		
	Yes	12	163.6	7.03	3.85	2.00	7.14

(Table 19 continued)

		No of cases	Person years	Rate (%)	IRR	95% CI Low	95% CI High
Mother smoking habit	Not at all	46	2020.1	2.25	1		
	Occasionally	10	518.7	1.95	0.87	0.42	1.78
	Daily	38	2057.9	1.85	0.82	0.51	1.32
Mother drinking habit	No	27	1403.8	1.91	1		
	Yes	60	2915.5	2.07	1.08	0.65	1.79
Child's physical activity level	More	26	1377.3	1.89	1		
	Equal	52	2329.4	2.22	1.18	0.68	2.05
	Less	6	194.9	3.17	1.68	0.62	4.56
Child's wheeze	No	83	4197.14	1.97	1		
	Yes	18	543.606	3.27	1.34	0.77	2.32
Dwell ownership status	No	43	2365.1	1.83	1		
	Yes	57	2363.0	2.41	1.32	0.85	2.04

* Normalized longitudinal weights were applied.

Table 20. Multivariate analysis of asthma incidence rate in Poisson model.*

		IRR	95% CI Low	95% CI High
Bio-mother's asthma history	No	1.00		
	Yes	4.54	1.32	16.12

* Normalized longitudinal weights were applied.

Table 21. Univariate analysis for the risk factors of wheeze incidence rate.*

		N of cases	Person years	Rate (%)	IRR	95% CI Low	95% CI High
Race of child	Aboriginal	97	2636.3	3.67	1		
	Non-Aboriginal	76	1536.9	4.93	1.34	0.91	1.96
Age of child	Infant/toddler	49	929.2	5.26	1		
	Pre-school	23	722.8	3.23	0.62	0.37	1.04
	School-age	102	2559.3	4.00	0.77	0.52	1.12
Sex of child	Female	83	2103.9	3.92	1		
	Male	92	2107.4	4.37	1.11	0.80	1.54
Sex of PMK	Female	139	3543.1	3.92	1		
	Male	36	668.3	5.35	1.37	0.86	2.18
Child allergy history	No	155	3860.6	4.01	1		
	Yes	19	262.6	7.2	1.75	1.02	3.03
Number of biological parents	Both	111	2545.7	4.38	1		
	One	27	701.7	3.89	0.89	0.53	1.5
	None	13	375.8	3.55	0.81	0.46	1.43
Mother education status	≥ High school	93	2490.6	3.72	1		
	≤ Secondary	68	1412.6	4.78	1.28	0.84	1.96
Number of older siblings	None	33	960.2	3.41	1		
	One	47	1279.6	3.64	1.08	0.65	1.79
	≥ Two	61	1140.9	5.38	1.59	0.95	2.68

		N of cases	Person years	Rate (%)	IRR	95% CI Low	95% CI High
Total household income	≤ 14,999	20	814.5	2.46	1		
	15,000 - 39,999	54	990.2	5.48	2.23	1.24	4.01
	≥ 40,000	100	2406.6	4.17	1.69	1.03	2.79
Territory of residence	Yukon	36	948.8	3.782	1		
	Northwest	95	1737.0	5.461	1.45	0.96	2.19
	Nunavut	44	1525.5	2.878	0.77	0.51	1.16
Region	Rural	68	2230.7	3.03	1		
	Urban	107	1980.6	5.41	1.79	1.23	2.56
Bio-mother's allergy history	No	115	2845.1	4.05	1		
	Yes	24	543.0	4.37	1.09	0.68	1.72
Bio-mother's asthma history	No	124	3235.5	3.84	1		
	Yes	15	152.6	9.50	2.50	1.35	4.55
Mother smoking habit	Not at all	73	1843.5	3.97	1		
	Occasionally	12	468.0	2.54	0.64	0.35	1.19
	Daily	84	1758.9	4.77	1.20	0.80	1.81
Mother drinking habit	No	46	1252.2	3.68	1		
	Yes	113	2559.7	4.4	1.19	0.81	1.75
Child physical activity level	Equal + less	93	2298.2	4.04	1		
	More	53	1231.4	4.34	1.08	0.69	1.67
Mother marital status	Married	156	3597.9	4.32	1		
	Single	10	297.3	3.34	0.78	0.39	1.54
	Widow	9	316.1	2.91	0.68	0.35	1.29
Dwelling ownership status	No	86	2120.8	4.03	1		
	Yes	86	2064.6	4.18	1.03	0.70	1.52

* Normalized longitudinal weights were applied.

Table 22. Multivariate analyses for the risk factors of wheeze incidence rate.*

		IRR	95%CI	
			Low	High
Age of child	Infant/toddler	1.00		
	Pre-school	0.45	0.23	0.90
	School-age	0.71	0.45	1.13
Child allergy History	No	1.00		
	Yes	2.04	1.14	3.70
Mother education Status	≥ High school	1.00		
	≤ Secondary	1.64	1.06	2.56
Number of older siblings	None + one	1.00		
	≥ Two	1.60	1.06	2.42
Total household Income	≤ 39,999	1.00		
	≥ 40,000	2.29	1.10	4.79
Territory of residence	Yukon + Nunavut	1.00		
	Northwest	1.78	1.15	2.76
Mother smoking Habit	No & Occasion	1.00		
	Daily	1.76	1.14	2.70

* Normalized longitudinal weights were applied.

Chapter 6

Discussion and Conclusion

The aim of this study was to investigate prevalence, incidence, and risk factors associated with asthma and wheeze in Aboriginal and non-Aboriginal children living in Yukon, Nunavut, Northwest Territories.

6.1 Validity of the current study

The dataset used in this thesis was derived from a longitudinal population-based survey, which had a complex sample design, with stratification, multiple stages of selection, and unequal probabilities of selection of respondents. Cross sectional and/or longitudinal weights were used in estimation and calculating variances. In order for prevalence and incidence rates of asthma to be free from bias, normalized cross-sectional and longitudinal weights were applied in all the estimations in the current study. Moreover, application of the longitudinal weights also allowed us to adjust the problem of loss to follow-up.

In the incidence study, of the 2,404 children who were studied in cycle 1, only 1,307 children were surveyed again in cycle 2 and/or cycle 3. We compared important factors associated with asthma and wheeze between the children who finished more than one cycle with those who completed only cycle 1. We found that several factors were significantly different between the two groups. Therefore, further exploration was carried out to assess possible effects of these unbalanced factors on the estimations. Four unbalanced risk factors, child allergy history, biological mother's asthma history, mother's daily smoking habit and child's age had significantly lower proportions or means in the children who completed more than

one cycle in comparison with those participated only in cycle 1. Since they were significantly lower among children included in the incidence study, their estimations were more likely to be under-estimated if all children would have been followed up for more than one cycle. Besides, although the means of child's age between the two groups were significantly different (5.12 years vs. 5.28 years, $p<0.05$), the difference in age was not clinically important. Even though total household income and territory of residence had significantly higher proportions in the children who completed more than one cycle in comparison with those finished only cycle 1, the proportions of total household income (≥ 40K) and residing in the NWT were similar (total household income: 54.81% vs. 54.19%; living in the NWT: 41.64% vs. 39.68%). Higher proportions of mother's education status (less than secondary) and number of older siblings in the children who completed more than one cycle in comparison with the children completed only cycle 1 might lead to over-estimation of risks.

Aboriginal children living in the three Northwest Territories are frequently seen by healthcare workers other than physicians or specialists. Consequently, the diagnosis of asthma in these children might be made by non-physicians. This in turn limits the validity of comparison of asthma prevalence and incidence in this study, compared to those reported for children living in other parts of Canada.

Despite the limitations discussed above, the study described in thesis made an attempt to describe prevalence, incidence and risk factors of asthma among Aboriginal children living in a remote area in Canada.

6.2 Asthma and wheezing prevalence

In this study, the prevalence of ever-asthma between the three territories were significantly different. NWT children had the highest prevalence of ever-asthma and

current-asthma. These geographical differences in asthma prevalence might be partially explained by the fact that NWT is more "urban" in comparison to the other two territories. Differences in prevalence of asthma between urban and rural have been identified in other studies (Aligne et al, 1999; Senthilselvan et al, 2003). In a study using the 1988 National Health Interview Survey to examine parental-report of current asthma in children aged 0 to 17 years, higher prevalence of asthma among black children was due to urban residence, and the authors concluded that all children living in urban areas regardless of their racial status were at increased risk for asthma (Aligne et al, 1999). Using a physician services database of the Saskatchewan Health Department from 1991 to 1998, others reported that physician diagnosed asthma prevalence was greater in urban populations than in rural populations for all age groups (Senthilselvan et al, 2003).

Prevalence of current-asthma and current-wheeze were found to be slightly greater in boys than in girls in the current study. This trend has been reported in several epidemiological studies independent of race and place of study (Sherriff et al, 2001; Senthilselvan et al, 2003; Bjornson et al, 2000). A birth cohort study conducted in UK, Avon Longitudinal Study of Parents and Children (ALSPAC) revealed that maternal reports of child wheeze which persisted between 0 to 6 months were significantly higher in boys compared to girls in the first three and half years of their lives (Sherriff et al, 2001). In Canada, gender differences in prevalence of asthma have also been reported among Aboriginal populations in Saskatchewan (Senthilselvan et al, 2003). Males are at greater risk of developing asthma than girls until approximately the age of puberty whereas, females are at greater risk after puberty. The reasons for the gender differences in asthma morbidity are not well understood; however, differences in hormonal changes between boys and girls at

puberty and smaller airways relative to lung volume in boys were discussed as possible pathophysiologic mechanisms for the gender differences in one review (Bjornson et al, 2000).

In this thesis, prevalence of ever-asthma in pre-school and school-age and prevalence of current-asthma in all age groups were higher in non-Aboriginal than Aboriginal children. Asthma hospitalization rates and prevalence were also reported to be lower in other non-Caucasian populations (The ISAAC Steering Committee, 1998; Whybourne et al, 1999; Chen et al, 2004). In the ISAAC study, cumulative prevalence of asthma was found to be lower in Asian and African countries (The ISAAC Steering Committee, 1998). Whybourne et al (1999) reported hospitalization rates from asthma in children aged 1 to 9 years living in Australia were significantly lower in Aboriginals and Torres Strait Islanders (ATSI) than non-ATSI (Whybourne et al, 1999). In a study of 287,329 children aged 0-14 years in China, asthma prevalence was found to be 1.50% (Chen et al, 2004), which was much lower than the corresponding asthma prevalence in developed countries including Canada. For example, 12.2% of Canadian children and youth < 20 years of age, and 14% of those 15-19 years old, report having physician-diagnosed asthma (Public Health Agency of Canada, 1999).

In this study, prevalence of wheeze was higher in Aboriginal children than non-Aboriginal children across all age groups and the difference reached significance in infants and toddlers, which was also true for both Aboriginal boys and girls. Moreover, this study showed that prevalence of ever-asthma in Aboriginal girls aged pre-school and under was higher than the corresponding non-Aboriginal girls. In a study of physician-diagnosed asthma among Registered Indian population in Saskatchewan, asthma prevalence rates for the Registered Indian population were

greater in preschool children aged 5 years and under and older adults aged 35 to 65 years (Senthilselvan et al, 2003). In another study conducted in Alberta, researchers reported that Aboriginal populations were more than two times more likely to visit Emergency Departments and physicians for asthma than non-Aboriginal population (Sin DD, 2002). A similar pattern was also observed in a study conducted among American Indian and Alaska Native children using Washington State hospitalization data for 1987 to 1996. In this study, there was no significant differences in asthma hospitalization rates in children aged 1 to < 5 years between American Indian and Alaska Native children and children in Washington State, whereas Indian and Alaska Native children aged under 1 year had two to three times higher rates of asthma hospitalization in comparison to overall asthma hospitalization rates in Washington State (Liu et al, 2000).

6.3 Factors associated with the prevalence of asthma and wheeze

In this study, the prevalence of ever-asthma was significantly associated with the biological mother's ever-asthma, the child's allergic history, territory and dwelling ownership. The prevalence of current-wheeze was significantly associated with being less than two years of age, having older siblings and having a mother who smoked. Biological mother's asthma history and child's allergic history have been frequently reported to be significant risk factors of asthma prevalence in children (Litonjua et al, 1988; Laitinene et al, 1998; Rasanen et al, 2000). Using a cross-sectional analysis of doctor-diagnosed asthma using data from a longitudinal birth cohort conducted in Boston, maternal asthma history was found to have stronger association with asthma prevalence than paternal asthma history among children younger than 5 years of age (Litonjua et al, 1988). A twin Finnish study found that among asthmatic children

with at least one asthmatic parent, genetic factors explained 87 percent of variation in susceptibility to asthma in twins (Rasanen et al, 2000; Laitinene et al, 1998). The child's allergic history is another important factor associated with asthma, and has been reported in many studies (Nickel et al, 2002; Illi et al, 2004). The MAS study reported that children with sensitization to food and/or common inhaled allergens during the first 3 years of life were at significantly higher risk of asthma at 7 years of age than those children with early transient or no sensitization (Nickel et al, 2002). In another report from the MAS study, children with early atopic dermatitis and concomitant wheeze were almost 3 times more likely to develop wheeze at age of 7 years in comparison to children without early atopic dermatitis (Illi et al, 2004).

Child's allergic history was also reported to be strongly associated with pediatric asthma among children from ethnical minority groups such as African American and Mexican American (Stevenson et al, 2001; Wong et al, 2001). A study of 4,164 children aged 6 to 16 years who participated in allergen testing in the Third National Health and Nutrition Examination Survey conducted in USA from 1988 to 1994 concluded that African American and Mexican American children were substantially more likely to be sensitized to allergens than Caucasian children (Stevenson et al, 2001). Children's allergy was also reported to be a significant risk factor for asthma in the countries where prevalence of asthma is very low. In a study of 10,902 school children aged 9-11 years in China, atopic sensitization, determined by skin-prick tests, was significantly associated with asthma (Wong et al, 2001).

Lack of dwelling ownership was a factor significantly associated with the prevalence of ever-asthma in the current study. This factor is closely related to socio-economic status (SES) of the household. Many research papers have reported that children from lower SES families were more likely to have asthma (Sherriff et al,

2001; Millar et al, 1998). The ALSPAC study reported that children living in rented local authority housing were at higher risk for wheeze that persisted beyond 6 months (Sherriff et al, 2001). In a large Canada-wide cross-sectional study of children aged 0 to 14 years, middle-income households had significantly low prevalence of asthma, compared with those in both lower- and higher-income households, and those children in lower-income households were more likely to have had a recent attack (Millar et al, 1998).

Overall, it is recognized that Aboriginal populations in Canada have lower income and over-crowded living conditions compared to non-Aboriginal population (Statistic Canada, 1999; Statistics Canada, 2001; Health Canada, 1999). Statistic Canada reported that 50.6% of Aboriginal people living in Calgary in 1995 reported low income in comparison with 20.6% low-income rate in general population in Calgary in 1995 (Statistic Canada, 1999). In 1991, average number of persons per occupied private dwelling for Registered Indian population on reserve was 4.1, compared to 2.7 for total Canadian population (Health Canada, 1999). In the 2001 Census, Aboriginal children aged 14 years and under were nearly twice as likely to live in crowded conditions than non-Aboriginal children (Statistics Canada, 2001). While 25% of Aboriginal children in non-reserve areas lived in crowded conditions in 2001, the comparable figure for all Canadian children in non-reserve areas was 13% (Statistics Canada, 2001). All of these SES factors might contribute to the observed association between lack of residence ownership and asthma prevalence. Moreover, there may be an association between airway irritants/allergen levels (such as dust) and home ownership. Further research in this area is needed.

Having more than two older siblings was a significant risk factor for prevalence of wheeze in the current study. Possible explanations for this association include

exposure to respiratory infectious diseases, which might stimulate wheezing (such as Respiratory Sinscitial Virus {RSV}). Having more siblings in the family, especially older ones, increases the chance of exposing younger children to infections (Ball, 2000; Sherriff et al, 2001; Yuan et al, 2003). The Tucson study reported that children with exposure to other children at home or at day care were more likely to have frequent wheezing at the age of two years than children with little or no exposure (Ball, 2000). The ALSPAC study reported that maternal reports of child wheeze, which persisted between 0 to 6 months, were significantly associated with presence of older siblings (Sherriff et al, 2001). A birth cohort study conducted in Denmark reported that children being second and third in the birth order were almost two times more likely to get both β-agonist and inhaled corticosteroid prescriptions for asthma in the first year of their lives (Yuan et al, 2003).

Maternal daily smoking was a significant factor associated with the prevalence of wheeze among Aboriginal children in the current study. This association was more prevalent among infants and toddlers (0 to < 2 yrs). The latter finding is not surprising since infants spend the majority of their time inside their homes, tightly linked to their mothers. Several studies have shown that parental smoking, especially maternal smoking, was a significant factor associated with asthma and wheezing among children (Kurukulaaratchy et al, 2003; Martinez et al, 1995). A birth cohort conducted in the United Kingdom reported that parental smoking before the age of 4 years was significantly associated with child's symptomatic bronchial hyper-responsiveness at 10 years of age (Kurukulaaratchy et al, 2003). The Tucson study reported that maternal smoking doubled the incidence of transient and persistent wheezing among children aged 0 to three years; however, showed weaker association among older children (Martinez et al, 1995). In a 1997 survey of First Nations and

Labrador Inuit individuals 15 years of age or older, 62% reported smoking regularly (Reading et al, 1999), which was two times higher than the rate of 29% reported for the general Canadian population in the same period (Statistics Canada, 1998).

6.4 Asthma and wheeze incidence rates

In this study, the NWT had higher incidence rates of asthma and wheeze in comparison with the other two territories. Incidence rates of asthma and wheeze were higher in non-Aboriginal children than Aboriginal children in all age groups. This trend was also true for both boys and girls. There have been limited studies of asthma incidence rates in Aboriginal children, and to the best of my knowledge, none has reported incidence rates of asthma in Aboriginal children.

6.5 Risk factors of incidence rates of asthma and wheeze

In this study, the biological mother's asthma history was a significant factor associated with asthma incidence. The child's age, child's history of allergy, maternal education status, number of older siblings, household income, territory and mother's smoking habits were significantly associated with wheeze incidence.

The history of childhood allergies has been reported to be a significant risk factor for wheeze and asthma incidence in several longitudinal studies (Lombardi et al, 1997 Ronmark et al, 2001). The Tucson study reported that skin test reactivity to allergens at age 6 was a significant risk factor for cumulative incidence of physician-diagnosed asthma at age 11 years (Lombardi et al, 1997). In a study of one-year incidence of physician-diagnosed asthma among children aged 7 and 8 years in Sweden, a positive skin test was significantly associated with asthma incidence (Ronmark et al, 2001).

Family history of asthma was an important risk factor for asthma incidence in the current study, which was also reported in a longitudinal study conducted in Sweden (Ronmark et al, 2001).

Age less than two years and the number of older siblings were two other factors found to be significantly associated with wheeze incidence in the current study. These two risk factors were also reported to be significant risk factors for wheeze incidence in the Tucson study (Ball et al, 2000), in which children with more exposure to other children at home or day-care were more likely to have frequently wheezing at the age of 2 years, but was likely to have frequent wheeze at from the age of 6 years (Ball et al, 2000).

Maternal smoking habits were significantly associated with wheeze incidence in the current study. It was also reported to be associated with 7-year cumulative incidence of physician-diagnosed asthma in children in a study conducted in Poland, in which the cumulative incidence rate was 2.0% in non-smoking families, 4.2% in one-parent-smoking families and 5.4% in two-parent-smoking families (Zejda et al, 2003).

In the current study, the mother's education status and household income were significantly associated with wheeze incidence. Previous studies have shown that low SES was a significant risk factor for asthma and wheeze incidence in adults (Eagan et al, 2004); however, to the best of our knowledge, no study has reported the association between asthma incidence and these two factors in children.

6.6 Limitations

There are several limitations that need to be considered in this report. The maximum length of follow-up was only six years in the current study. This resulted

in limited data for adolescents and changes in risk factors during the transition from childhood to adolescents were not examined. The longitudinal part of the study had a relatively small sample size due to attrition. Smaller sample size for the longitudinal study prevented us from completing subgroup analysis and reduced the statistical power of detecting small differences.

The survey was a general health survey and did not focus on asthma and/or wheeze specifically. This limited the depth of the asthma and wheeze analysis that could be completed. In the current study, parental report of physician-diagnosed asthma was used to determine asthma prevalence and incidence. Although parental report of physician-diagnosed asthma is frequently used in epidemiological studies, the validity of asthma diagnosis has been questioned. However, parental-report of physician-diagnosed asthma has shown to have good agreement with lung function measurements in adults (Senthilselvan et al, 1993) and with physician examination in children (Rennie, 1996).

Bootstrap weights were not available for the cross-sectional and longitudinal analysis conducted in the current study. Use of the bootstrap weights would have improved the estimations of standard errors, which were utilized in determining the significance of risk factors.

6.7 Conclusion

In conclusion, among children residing in Yukon, Nunavut and Northwest Territories, the prevalence of current-wheeze in Aboriginal infants and toddlers was significantly higher than non-Aboriginals. The prevalence of ever-asthma and incidence of wheeze in Aboriginal girls aged pre-school and under were higher than the corresponding non-Aboriginal girls. Non-Aboriginal school-age children had

significantly higher asthma and wheeze incidence rates than the corresponding Aboriginal children.

Several risk factors were associated with the prevalence and incidence of asthma and wheeze in children residing in the Territories. Maternal history of asthma was a significant factor for prevalence and incidence of asthma, and incidence of wheeze. Being infants and toddlers, a higher number of siblings and the mother's smoking habit were significantly associated with the prevalence and incidence of wheeze. The child's allergic history was a significantly associated with the prevalence of asthma and incidence of wheeze. Dwelling ownership, an indicator of socio-economic status, was significantly associated with prevalence of asthma while mother's educational status and total household income were significantly associated with incidence of wheeze.

Results from our study will enhance the understanding of epidemiology of asthma in rural Canadian children, including those of Aboriginal race. Generalization of the results from the incidence study was limited by the small sample size and high attrition rates and further research is required to confirm the findings.

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Appendix

Abbreviations used in this study

Abbreviation	Description
Age	Child's age
Bio-mother	Biological mother
Child's language	Child first language
Gender	Child's gender status
Infants/toddlers	0 to < 2 years
IRR	Incidence rate ratio
Marital status	Mother's marital status
NLSCY-north	National longitudinal survey of children and youth-north
NWT	Northwest territories
PMK	Person most knowledgeable about the child
Pre-school	2 to < 5 years
PSU	Primary Sampling Unit
PY	Person years
Race	Child's racial status
School-aged	5 to < 12 years
SES	Social economic status
Stratified analysis	Introduction of an interaction term between race and significant factors